DEPARTMENTS OF LABOR AND HEALTH, EDUCATION, AND WELFARE APPROPRIATIONS FOR 1975

U.S. House Congress. House. Committee on
Appropriations

HEARINGS

BEFORE A

SUBCOMMITTEE OF THE COMMITTEE ON APPROPRIATIONS HOUSE OF REPRESENTATIVES

NINETY-THIRD CONGRESS

SECOND SESSION

SUBCOMMITTEE ON DEPARTMENTS OF LABOR AND HEALTH,
EDUCATION, AND WELFARE APPROPRIATIONS

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PART 4

NATIONAL INSTITUTES OF HEALTH

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PART 4

NATIONAL INSTITUTES OF HEALTH

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DEPARTMENTS OF LABOR AND HEALTH, EDUCATION, AND WELFARE APPROPRIATIONS FOR FISCAL YEAR 1975

MONDAY, MARCH 25, 1974

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

NATIONAL INSTITUTES OF HEALTH

Testimony of Director

WITNESSES

DR. ROBERT S. STONE, DIRECTOR, NATIONAL INSTITUTES OF HEALTH

DR. DeWITT STETTEN, JR., DEPUTY DIRECTOR FOR SCIENCE, NATIONAL INSTITUTES OF HEALTH

DR. THOMAS E. MALONE, ASSOCIATE DIRECTOR FOR EXTRAMURAL RESEARCH AND TRAINING, NATIONAL INSTITUTES OF HEALTH

DR. MARTIN M. CUMMINGS, DIRECTOR, NATIONAL LIBRARY OF MEDICINE

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CHARLES MILLER, DEPUTY ASSISTANT SECRETARY, BUDGET

Mr. Flood. Today we have the National Institutes of Health. The presentation is to be made by the Director, Dr. Stone. We have a biographical sketch of you, Dr. Stone, which we will place in the record at this point.

[The biographical sketch follows:]

Department of Health, Education, and Welfare, National Institutes of Health, Biographical Sketch

Name: Robert S. Stone, M.D.
Position: Director, National Institute of Health
Birthplace and date: New York, N.Y., February 10, 1922
Education:
  A.B., Brooklyn College, Brooklyn, N.Y., June 1942
  M.D., State University of New York College of Medicine, Brooklyn, N.Y., June 1950

Experience:
- 1973–Present: Director, National Institutes of Health, Bethesda, Md.
- 1972–73: Visiting Professor, Sloan School of Management, Mass., Institute of Technology
- 1971: Member, Governor's Task Force on Drug Abuse
- 1971: Member, Board of Directors, Mid-Rio Grande Health Planning Council, Inc., Albuquerque, N. Mex.
- 1971: Member, Policy Board, Drug Abuse Education and Coordination Center, Albuquerque, N. Mex.
- 1971: Member, Advisory Committee on Undergraduate Medical Education Council on Medical Education, AMA
- 1971: Member, National Advisory Council on Health Professions Education Assistance, NIH.
- 1970: Member, National Policy Board, Los Alamos Meson Physics Facility
- 1970: Member, Grant Review Committee, National Fund for Medical Education
- 1970: Member, Editorial Board, Journal of Medical Education
- 1970–71: Member, Council of Deans Administrative Board, Association of American Medical Colleges
- 1970: Vice President for Health Sciences, University of New Mexico, Albuquerque, N. Mex.
- 1968: Member, Executive Committee, New Mexico regional medical program
- 1968: Dean, School of Medicine, University of New Mexico, Albuquerque, N. Mex.
- 1968: Consultant, Bureau of Health Professions Education and Manpower Training, National Institutes of Health, Bethesda, Md.
- 1967–69: Consulant, Public Health Service, district IV regional office
- 1967: Consultant, Atomic Energy Commission, Los Alamos Scientific Laboratory, N. Mex.
- 1966–68: Associate Dean, School of Medicine, University of New Mexico, Albuquerque, N. Mex.
- 1965–69: Consultant, William Beaumont General Hospital, El Paso, Tex.
- 1963: Consultant, Albuquerque Veterans Administration Hospital, N. Mex.
- 1963–68: Chief, Pathology, Bernalillo County-Indian Hospital, Albuquerque, N. Mex.
- 1963–68: Professor and chairman, Pathology, School of Medicine, University of New Mexico, Albuquerque, N. Mex.
- 1958–63: Pathologist, Shriners Hospital for Crippled Children, Los Angeles, Calif.
- 1957–59: Deputy coroner, Los Angeles County, Calif.
- 1955–63: Attending physician, Los Angeles County Harbor General Hospital, Torrance, Calif.
- 1955–63: Attending physician, Sawtelle Veterans Administration Center; Los Angeles, Calif.
- 1952–63: Instructor to associate professor in pathology, University of California School of Medicine, Los Angeles, Calif.
- 1950–52: Internship and assistant residency in pathology, Presbyterian Hospital, New York, N.Y.
- 1950–51: Instructor in pathology, Columbia University College of Physicians and Surgeons, New York, N.Y.
- 1949: Assistant in pathology, Brookhaven National Laboratory, Upton, Long Island, N.Y.
- 1948: Instructor in biology, Brooklyn College, N.Y.
- 1942–46: Ensign, U.S. Navy (Epidemiology)

University appointments:
- 1970: Building committee (UNM), Albuquerque, N. Mex.
- 1965: President's Ad Hoc Advisory Committee on Computer Facility Development (UNM), Albuquerque, N. Mex.
- 1964–65: Research Allocations Committee (UNM), Albuquerque, N. Mex.
- 1961–63: Curriculum and Educational Policy Committee, School of Medicine (UCLA), California.
- 1958: Chairman, Chancellor's Ad Hoc Committee on Interdisciplinary Exchange Program between Law School and Medical School (UCLA).
- 1958: Medical Education for National Defense Committee, Medical School (UCLA), California.
- 1957: Building Committee, School of Public Health & Occupational Medicine.
- 1954–59: Internship and residency committee, medical school UCLA).

Professional and scientific memberships:
  Albuquerque and Bernalillo County Medical Association (various committees). Member, board of trustees, 1970; member, planning committee, 1970, New Mexico.
  American Association of Chairmen of Medical School Departments of Pathology (1965–68); president, 1967.
  American Association of Pathologists and Bacteriologists.
  American Medical Association.
  American Society for Cell Biology.
  American Society for Experimental Pathology.
  College of American Pathologists, fellow (1956–70).
  Electron Microscopy Society of America.
  New Mexico Medical Society (various committees).
  New Mexico Society of Pathologists.
  Executive council, Association of American Medical Colleges, 1972–.
Honors:
  1948: Alpha Omega Alpha.
  1950: Reverend Chauncey Mitchell Prize, State University of New York, Downstate, "best qualified in all departments of medicine."
  1970: Albuquerque Jaycees, Distinguished Public Service Award.
  1971: New Mexico Board of Realtors, New Mexico Citizen of the Year.

CURRICULUM VITAE

Name: DeWitt Stetten, Jr.
Home address: 14 North Drive, Bethesda, Md. 20014.
Date and place of birth: New York City, May 31, 1909.
Family: Marjorie Roloff Stetten, wife. Four children.
Education:
  A.B., Harvard College, 1930.
  M.D., Columbia University, 1934.
  Ph. D. (biochemistry), Columbia University, 1940.
Special training or experience:
  1934–37: Intern, resident, Bellevue Hospital, New York City.
  1947–49: Associate in medicine, Peter Bent Brigham Hospital.
  1952–53: Study section on nutrition and metabolism, National Institutes of Health, Public Health Service.
Chronology of employment:
  1938–47: Assistant, instructor, assistant professor, department of biochemistry, Columbia University.
  1947–48: Assistant professor, department of biochemistry, Harvard University.
  1948–54: chief, division of nutrition and physiology, Public Health Research Institute of City of New York, Inc.
  1954–62: Associate Director in Charge of Research, and Chief, Section on Intermediary Metabolism, National Institute of Arthritis and Metabolic Diseases, National Institutes of Health.
  1962–70: Dean, Rutgers Medical School and director of medical center.
  1970–74: Director, National Institute of General Medical Sciences, National Institutes of Health.
  1974–: Deputy Director for Science, National Institutes of Health.
Organizations:
  American Academy of Arts and Sciences.
  American Association for the Advancement of Science (fellow) (VP 1962).
  American Institute of Chemists (fellow).
  American Society of Biological Chemists.
  Harvey Society.
  Phi Beta Kappa.
  Alpha Omega Alpha.
  Sigma Xi.
  Society of Experimental Biology and Medicine.
Offices held:
  1948–49: Subcommittee on Liver Diseases, National Research Council.
  1948–52: Panel on Intermediary Metabolism, Committee on Growth, National Research Council (Chairman 1950).
  1948–53: Consultant, Walter Reed Army Medical Center.

1951–52: Chairman, Research Committee, New York Diabetes Association.
1953–54: Consultant, NIH, Bethesda, Md.
1966–70: Chairman, Scientific Advisory Committee, Roche Institute of Molecular Biology.
1971–73: Vice President, Foundation for Advanced Education in the Sciences.
1973–74: President, Foundation for Advanced Education in the Sciences.

Member:
- Advisory Board, American Journal of Medicine.
- Advisory Board, Perspective in Biology and Medicine.
- National Advisory Committee, Oklahoma Foundation for Medical Research.
- Advisory Committee, Department of Biology, Princeton University.
- Board of Directors, Foundation for Advanced Education in the Sciences.
- Executive Committee, Division of Medical Sciences, National Academy of Sciences, National Research Council, 1966–70.
- National Advisory General Medical Sciences Council, NIH, 1968–70.

Honors and other special scientific recognition:
- Harvard College scholarships, 1927 and 1929.
- Columbia University fellow, 1939.
- Joseph Mather Smith Prize, 1943.
- Alvarenga Prize Award, 1954.
- Horace Mann Award for Outstanding Alumnus of the Year, 1957.
- Banting Medal from the American Diabetes Association, 1957.
- DHEW Superior Service Honor Award, 1973.

DR. THOMAS E. MALONE, ASSOCIATE DIRECTOR FOR EXTERNAL RESEARCH AND TRAINING

June 3, 1926, Henderson, N.C., married, two children.

Education: Morehouse College, 1943–45. B.S., North Carolina College, 1948. M.S., North Carolina College, 1949. Ph. D., Harvard University, 1952.

Professional history: 1950–52, teaching fellow, Harvard University, Cambridge, Mass. 1952–58, assistant professor of zoology, North Carolina College, Durham, N.C. 1957, 1958 (summers), lecturer in National Science Foundation Institutes for High School Teachers of Science and Mathematics. 1958–60, resident research associate, Argonne National Laboratory. (Postdoctoral fellowship recommended by National Academy of Sciences-National Research Council.) 1960, National Science Foundation Panelist for reviewing proposals submitted for projects in science education and research. 1960, assistant professor of biology, Loyola University, Chicago, Ill. 1961 (summer), visiting lecturer, Sabin Branch Chicago Teachers College, Chicago, Ill. 1961–62, visiting lecturer, evening division, Illinois Institute of Technology, Chicago, Ill. 1962 (summer), director, Summer Science Training Program for High-ability Secondary School Students of Loyola University, Chicago, Ill. (sponsored by the National Science Foundation). 1962, Grants Associate, DRG, NIH. 1963–64, Assistant Chief, Research Grants Section, EP, NIDR, NIH. 1964–66, Deputy Chief, EP, NIDR, NIH. 1966–67, Chief, Periodontal Diseases and Soft Tissue Studies, EP, NIDR, NIH. 1967–69, Chairman, Department of Biology, American University of Beirut, Beirut, Lebanon. 1969–72, Associate Director for Extramural Programs, NIDR, NIH. August 1972 to present, Associate Director for Extramural Research and Training, NIH.

Professional organizations: American Association for the Advancement of Science, New York Academy of Sciences, American Society of Zoologists, the Histochemical Society, American Society for Cell Biology, International Association of Dental Research, Sigma Xi.

Honors, awards:
- Harvard Fellow, 1950–52.
- NAS–National Research Council Fellow, 1958–59.
- DHEW Superior Service Award, 1970.

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

PUBLIC HEALTH SERVICE, NATIONAL INSTITUTES OF HEALTH

BIOGRAPHICAL SKETCH

Name: Leon M. Schwartz
Position: Associate Director for Administration, NIH

Birthplace and date: Baltimore, Md., April 26, 1928
Education: A.B., Economics, Johns Hopkins University, 1950
Experience:
- Associate Director for Administration, NIH, January 1972–present
- Deputy Assistant Director for Program Management, Research Applications Directorate, National Science Foundation, 1971
- Assistant Commissioner for Administration, Office of Education, DHEW, 1968–71
- Deputy Assistant Commissioner for Administration, Office of Education, DHEW, 1967–68
- Goddard Space Flight Center, National Aeronautics and Space Administration, 1960–67
  - Chief of Program Review and Resources Management, 1966–67
  - Director of Program Support Division, 1965–66
  - Business Manager, meteorology satellite program, 1962–65; financial cost analyst, 1960–62
- Assistant Treasurer and Chief Accountant, Carpel, Inc., 1954–60
- Part-time instructor, accounting—Pace Accounting Course, Baltimore Institute, 1958–63

Association Memberships: Maryland Association of Certified Public Accountants
Special Awards, Citations or Publications: Certified public accountant, HEW superior service award, 1970; Consultant to National Science Foundation, Advisory Panel for the research management improvement program, 1973–74

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

NATIONAL INSTITUTES OF HEALTH

BIOGRAPHICAL SKETCH

Name: Thomas J. Kennedy, Jr.
Position: Associate Director for Program Planning and Evaluation, OD
Birthplace and date: Washington, D.C., June 24, 1920
Education: Catholic University of America, Washington, D.C., B.S., 1940; Johns Hopkins University, Baltimore, Md., M.D., 1943
Experience: Associate Director for Program Planning and Evaluation, Office of the Director, NIH, September 1968–present; Director, Division of Research Facilities and Resources, NIH, 1965–September 1968; Special Assistant to the Director for Scientific Communications, Office of the Director, NIH, 1962–65; Assistant to the Director of Laboratories and Clinics, Office of the Director, NIH, 1960–62; attending physician and responsible clinical investigator, National Heart Institute, NIH, 1953–60; Investigator, Laboratory of Kidney and Electrolyte Metabolism, National Heart Institute, NIH, 1950–60; associate (research) in medicine, George Washington University School of Medicine, Washington, D.C., 1951–65; S.A. surgeon—Medical Director, U.S.P.H.S., 1950–present; research fellow, research service, First (Columbia) Medical Division, Goldwater Memorial Hospital, New York City, 1949–50; assistant in medicine, Columbia University College of Physicians and Surgeons, New York City, 1948–50; resident physician, research service, First (Columbia) Medical Division, Goldwater Memorial Hospital, New York City, 1947–49; research fellow, NYU College of Medicine, New York City, 1945–47; research fellow, research service, 3rd (NYU) Medical Division, Goldwater Memorial Hospital, New York City, 1945–47; first lieutenant and captain, AUS, assigned to Office of Scientific Research and Development, 1944–47; Intern, medical service, Peter Bent Brigham Hospital, Boston, Mass. 1944.
Association memberships: American Federation for Clinical Research, American Physiological Society; American Board of Internal Medicine.

Dr. STONE. If I may begin.

Mr. FLOOD. Yes, I see you have a prepared statement.

Dr. STONE. Yes, sir.

Mr. FLOOD. Do you want to proceed with that?

Dr. STONE. Yes, sir.

OPENING STATEMENT

Mr. Chairman and members of the committee: Before embarking on a general overview of the budget estimates for the National Institutes of Health, I should like to introduce our new Deputy Director for Science—Dr. DeWitt Stetten who, as you know, has been director of the National Institute of General Medical Sciences since 1970. Dr. Stetten has a broad background in research and in academic medicine. He did his undergraduate work at Harvard, earned his MD degree and a Ph. D. at Columbia University and subsequently had appointments as assistant professor of biochemistry both at Columbia and at Harvard. After serving for 6 years as the Chief of the Division of Nutrition and Physiology in the Public Health Research Institute of New York City, he joined NIH, in 1954, as director in intramural research in what was then the National Institute of Arthritis and Metabolic Diseases. From 1962 until his return to NIH in 1970, he was the first dean of the new Rutgers Medical School. In his new position, Dr. Stetten's main responsibility is for the intramural research programs and their supporting services.

Dr. Stetten succeeds Dr. Robert Berliner who retired, after 24 years of service at NIH, first as a distinguished research scientist and later as an effective and even-handed administrator, in order to become the dean of the medical school at Yale University.

As the Directors of the several NIH components—the 10 Institutes, the Division of Research Resources, the Fogarty International Center, and the National Library of Medicine—will discuss their respective activities and testify in support of the relevant appropriation requests, I should like to deal briefly with the NIH budget as a whole and to discuss two aspects of this year's justifications that are common to all of the NIH components and are therefore most easily dealt with at this point in the hearings. These two aspects are:

The purpose and significance of the new budget format, and
The status of the research training programs.

BUDGET ESTIMATES

The budget estimates for NIH that are now before you are in a new format that highlights the nature of the research supported by the extramural programs rather than the form in which the support is provided. In other words, the activity structure of the budget presentations for each of the Institutes is primarily focused on the disease or scientific research areas with which the Institute is concerned—such as digestive diseases, neurological disorders, vital diseases, genetics, aging, glaucoma, and so forth—rather than on the allocation of funds to the various support mechanisms—that is, regular research grants, center grants, training grants, fellowships, and research contracts. This format was suggested by NIH after a fairly intensive review of various aspects of program management, by an inter-Institute committee, and after considerable internal discussion.

NEW BUDGET FORMAT

One of its purposes is to give greater visibility to the areas of research with which the Institutes are actively concerned and to give rough measure of the relative effort devoted to each—at least in terms of funds expended. It can only be a rough measure because the "program activities" displayed are limited to major areas of concern, in order to avoid unmanageably detailed tables, and it is, of course, true that not all research projects will fit neatly into the categories thus selected. It must also be borne in mind that much research—especially research that, for want of a better name, is usually described as "basic research"—is equally relevant, or, at least, potentially relevant, to a number of research areas and must, therefore, be somewhat arbitrarily included in one of several possible "program activities." In any case, a more or less accurate classification of work supported can only be retrospective. The allocation of future funds to the various "program activities" is thus partly a reflection of how funds were deployed in previous years but, more importantly, it is also an indication of each Institute's judgment on the relative emphasis appropriate to various parts of its mission. Such judgment is based on assessments both of opportunity and of need by the Institute's professional staff and its outside advisers. In fact, the management staff for the extramural programs is gradually being reorganized to reflect the new activity structure so that a program manager will, in future, be responsible for both grants and contracts in a particular program area rather than for just grants or contracts in a hodgepodge of program areas.

I am well aware that this new arrangement may seem to imply a much greater emphasis on so-called "targeted" research. This, however, is not the case. All of the research supported by NIH is targeted in the sense that it is undertaken in the expectation that it will, ultimately, contribute to the development of better preventive, diagnostic or therapeutic measures. That, indeed, is the mission of each of the institutes and research which does not have this aim is clearly not eligible for NIH support. But this mandatory mission-orientation does not, in any way, run counter to the concern expressed by this committee in its report on last year's appropriation bill [p. 23–24] that "the most productive approach to research in medicine . . . is through the unfettered initiative of independent investigators" or its valid skepticism "that program managers in Washington or Bethesda . . . are better able to determine the proper scope and direction of research projects than scientists and physicians who are actively engaged in the pursuit of knowledge." It is as much our intent as it is this committee's view "that the regular research grant program of NIH, in which awards are made on the basis of an evaluation of the scientific merit of the proposal and the professional competence of the investigator by a committee of his peers, must remain the hard core of the national biomedical research effort." In short, the new budget format does not reflect or presage a change in program orientation—it is merely a change in budget presentation which, we believe, makes the scope of NIH's research-support more readily intelligible.

BASIC RESEARCH

In this connection, I should also emphasize that there has been no retreat from our strongly held conviction that major progress in the fight against disease and disability will depend on a much better understanding than we now have not only of their cause and nature but also of the intricacies of biological processes and the impact on them of environmental factors. The painstaking development of such understanding, the search for basic principles, and the discovery of the many persistent and elusive biological secrets is the task of basic research—a task to which NIH must remain firmly committed. This, as you know, is the unshakeable and often passionately defended view of almost all research scientists. It is also, I am glad to say, the policy of this administration. You will have noted that the President, in his health message sent to the Congress on February 20, said:

> In addition to attacking problems of the delivery system as a means of improving our health care, we must also continue to support our basic scientific research. It is this work that will tomorrow yield the remedies to diseases that affect our people.

And I should like to add that this passage was not drafted or suggested by NIH. Dr. Edwards, in his talk to the NIH staff on February 21, also emphasized that the administration of NIH programs should be designed to "keep the focus of NIH properly trained on fundamental research." That is certainly our intent because there is no doubt whatever about its usefulness and, indeed, its essentiality.

EXAMPLE OF BASIC RESEARCH RESULTS

Let me cite one current example of the practical results flowing from a basic research project. For the past 15 years a group of NIH scientists, under the direction of Dr. Roscoe Brady, in the Neurology Institute have been studying fatty molecules—so-called lipids—that exist in the brain. They were interested in discovering how these molecules were manufactured by the brain, where they were used in the brain cells, and how the brain disposed of them. I shall not attempt to describe 15 years of complex research in a few simple sentences, so let me just say that a link was eventually established between this work and a group of inherited diseases—of which 10 have so far been identified—that almost always result in death early in childhood due to an accumulation of fatty molecules in the cells of the brain, the liver, the spleen and other organs. In order to examine the nature of the abnormalities in these lipid storage diseases, the group needed special radioactive chemicals that would allow them to label and follow the formation and degradation of the various individual fatty components. These were obtained, rapidly and relatively inexpensively under a Public Law 480 counterpart funds contract, from the world's leading authority on the chemical synthesis of this class of components—a scientist at the Weizmann Institute in Israel. I may say, parenthetically, that this is an excellent example of the effectiveness and importance of the Public Law 480 program.

LIPID STORAGE DISEASES

Dr. Brady's group has now identified the specific abnormality that is responsible for each of the major lipid storage diseases—notably, Gaucher's, Niemann-Pick, Fabry's and Tay-Sachs diseases. In each case, an enzyme that is essential in the sequence of steps for degrading and disposing of the complex lipid compounds is either missing or ineffective as the result of a genetic defect. When these enzymes had been identified, it was possible to devise relatively simple methods not only for diagnosing patients but for identifying carriers of these diseases who may transmit them to their children. These diagnostic tests, which in most cases merely consist of determining the presence or absence of the specific enzyme in white blood cells from a small sample of blood, are very specific and reliable and have been carried out on literally thousands of samples sent in from patients all over the world. In addition, Dr. Brady's group has adapted the tests to samples of amniotic fluid obtained from the mother's womb to determine whether a baby, one of whose parents is a carrier of one of these diseases, is actually at risk. Enough of these pregnancy tests have been done to validate this procedure and to permit effective genetic counseling for the parents.

Finally, the NIH investigators have now succeeded in purifying from normal human placenta several of the enzymes that are missing in these lipid storage diseases. Trials of enzyme replacement therapy have been carried out on patients with Gaucher's and with Fabry's disease. While it is too early to tell whether long-term benefits will ensue, the biochemical abnormalities in the blood and liver in these patients were significantly ameliorated.

In the case of Tay-Sachs disease—which is as peculiar to Ashkenazi Jews as sickle-cell anemia, generally, is to blacks—the situation is complicated because two forms of the enzyme are involved. Both forms have been purified by Dr. Brady's group but it is not certain whether simple enzyme replacement therapy will be effective because the organ primarily affected is the brain and it is very difficult to deliver the large protein molecules that form these enzymes directly to the brain. However, the isolation of these two Tay-Sachs enzymes explains why there are four variants or forms of the disease since genetic mutations can alter or delete different combinations of these two enzymes. This last finding has very practical implications for diagnostic screening of suspected patients. The usual diagnostic tests have used an artificial chemical, rather than the natural fatty compound, and it is now clear that in at least two of the Tay-Sachs variants only the natural compound will yield a correct diagnosis. Consequently, the group has turned again to their collaborator in Israel for the development of large-scale production methods for the natural compound needed for these diagnostic tests.

In addition to the direct relevance of this basic research to the lipid-storage diseases, which are relatively rare, it has raised the possibility that inherited enzyme deficiencies may also play an unsuspected role in other diseases and abnormalities. Indeed, analogous work is being done by Dr. Elizabeth Neufeld, in the Heart Institute, on a group of diseases—with the jaw-breaking name of mucopolysaccharidoses—that, among other things, cause deformities in children.

I have described this work, its consequences to date, and its promise for the future because it illustrates several points I should like to make. It is an excellent example—but certainly not an unusual one—of the practical results flowing from work which, at its inception and through much of its earlier stages, might well have been considered rather esoteric and with no foreseeable application. It is an excellent example of the importance of international cooperation in research, and especially of the value of the Public Law 480 program, whose foreign currencies will, unfortunately, soon be exhausted. It is an excellent example—and again, far from an unusual one—of the competence, the ingenuity, the perserverance, and the effectiveness of the scientists and clinicians who staff the intramural programs that have earned for NIH its high reputation and worldwide renown.

INTRAMURAL PROGRAMS

As a newcomer to NIH and as an administrator who is not an alumnus of its intramural program, I think I can be quite objective when I say that during the past 9 months, while familiarizing myself with the work being done at NIH, I have been tremendously impressed by the high quality of the staff, their dedication to their tasks, and their pride in and loyalty to the National Institutes of Health. It is quite clear that the scientists and their assistants working at NIH are continuing to build its reputation and are not just coasting on it. I have been reminded that for 59 years after the Laboratory of Hygiene was established on Staten Island, in 1887, for research on cholera and other infectious diseases, NIH and its antecedents were engaged solely in intramural research. Only since 1946, when a Research Grants Office was set up, has NIH had a significant extramural program. This program now absorbs more than 80 percent of the budget but involves only 20 percent of the staff. In many ways, it remains an appendage grafted onto a flourishing research institution. Because of our preoccupation with the larger and more troublesome extramural activities, the tail often seems to wag the dog, but there is little doubt that its brain—and its bite—are still firmly fixed in its head.

TRAINING GRANTS AND FELLOWSHIPS

The status of the training grant and fellowship programs has been somewhat complicated by a series of events of which you are, I am sure, already aware. The new program, announced by Secretary Weinberger last July, envisages a phaseout of research training grants, as current commitments expire, and a substantial increase in the number of research fellowships and in the size of the stipend. These fellowships will be entirely at the postdoctoral level and will, for the most part, be made directly to the individual fellow on the basis of national competition. However, in order to enable nonprofit institutions to develop a research training capacity and opportunities for training individuals in particular health sciences or related fields in which there is a manpower shortage, there will be a limited number of institutional research fellowship awards for which the fellows will be selected by the preceptor. No training for clinical practice—so-called specialty training—will be permitted under the new program.

The phaseout of the old program has, of course, been postponed by the court order to release some of the fiscal year 1973 funds that had not been obligated and the subsequent release of all previously withheld fiscal year 1973 funds. As a result, 152 additional new training grants were awarded and paid from released fiscal year 1973 funds, and supplemental awards were made to existing training grants for the support of additional trainees when the ban on the appointment of new trainees was rescinded. It is estimated that support will thus be provided for an additional 4,690 trainees (full-time equivalent), bringing the total supported from fiscal year 1973 funds to 13,409. Similarly, an additional 680 fellowships will probably be awarded, bringing the fiscal year 1973 total to 1,831.

Under the guidelines for the new program, approximately 2,000 fellowships will be awarded from fiscal year 1974 funds, and 1,410 training grants will be made as part of the phaseout commitment.

The budget request for fiscal year 1975 envisages a further increase of fellowships to 4,226, at a cost of $61.2 million. Training grants will continue at a reduced level of 971 awards costing $61.1 million. These training grants will provide support for 7,435 trainees (full-time equivalent). The total number of individuals receiving research training will thus be 11,662—an increase of 1,162, or 10 percent, over the 10,500 supported from fiscal year 1974 funds.

A proposal to reconcile the differences between the old training program and new program launched in fiscal year 1974 and thus to merge them into a single new program is being held in abeyance pending a decision by the Congress on H.R. 7724, the Rogers-Kennedy research training bill.

RESEARCH TRAINING PROGRAM

In view of this committee's repeatedly expressed concern about the future of the research training programs, I should like to emphasize that a decision to continue the research training program has been made that it is not intended, as the committee at one time feared, to phase out training altogether. The distinguishing feature of the new approach announced by Secretary Weinberger is that support will be selectively provided direct to the individuals to be trained through competitive fellowships rather than through training grants.

BUDGET ESTIMATE FOR NIH

The budget request for NIH, as a whole, reflects the administration's continued commitment to the support of biomedical research. The estimates total $1,834,784,000, an increase of a little more than $54 million over the comparable fiscal year 1974 figure. The budget also reflects the President's decision—reaffirmed in his health message—that the conquest of cancer is a national goal and that research on heart, blood vessel, lung, and blood diseases must have increased attention. Accordingly, the budget requests $600 million for the National Cancer Institute, an increase of $72.6 million or 14 percent; and $309.3 million for the National Heart and Lung Institute, an increase of $22.6 million or 8 percent. For the Cancer Institute, the increase will be divided as follows:

The amounts of $24.1 million for research on the treatment of cancer; $16.9 million for research on cause and prevention; $12.5 million for cancer biology; $11.2 million for cancer control; $5.6 million for detection and diagnosis research, and $3.9 million for cancer centers support.

The Heart and Lung Institute will continue to emphasize studies on blood resources; will continue to seek out new modes of therapy for the treatment of sickle-cell crises, as well as fund comprehensive research centers for sickle-cell disease; and establish additional research and demonstration centers.

The estimates for the other research institutes are virtually the same as for last year, though it must be pointed out that within the institute totals there are a number of significant increases for some program activities that are offset by reductions in others.

There is an increase of $1.5 million, or 6 percent, for the National Library of Medicine; and an increase of $5.1 million, or 40 percent, for the Office of the Director—the latter, however, is almost entirely for the payment of rent to the General Services Administration.

GENERAL RESEARCH SUPPORT GRANTS

The only major decrease—$44.2 million in the estimate for the Division of Research Resources—results from the decision to discontinue the general research support grants. As was explained at last year's hearings, these grants served a useful purpose when total research funds were smaller and when many institutions were still in process of building up their research capabilities. The conditions that led to the inauguration of this program in 1961 no longer obtain in 1974, and these grants can no longer be regarded as an essential part of biomedical research support. The formula by which the amount of these grants was computed favored institutions that were already receiving the larger amounts of research support, and this makes it very difficult to justify continuation of the program when it is also necessary to allocate additional funds to specific categorical research programs with national importance in the fight against such ubiquitous killers as heart disease and cancer. However, the new minority schools biomedical support program—which was the part of the general research support grant program designed to assist minority institutions to build up their research capabilities—will be continued.

I do not pretend to be wholly satisfied with our budget requests and I do not expect that I ever will be. There is so much to be done in medical research that no rational increases in the NIH budget will ever suffice to meet all demands or satisfy all worthy claimants for support. At the same time, $1.8 billion is a very large sum of money and represents an investment in biomedical research that is not matched, on a per capita or any other comparable basis, in any other country. It is, I am sure, a sound investment and one from which all mankind will profit.

Mr. Flood. Doctor, most of us on this committee are not amateurs in this business, as you know.

Dr. Stone. Yes, sir.

EMPLOYEE MORALE

Mr. Flood. Most of the impetus for the creation and the growth of NIH came from the Congress and not from the executive branch. We regard NIH as our baby and we take a great deal of pride in achievements in biomedical research which have come about as a direct result of NIH support down through the years.

As a matter of fact, we are very gratified from time to time—and we make no bones about saying so—when we hear of some scientist who has won the Nobel Prize, or some such award under the auspices of the NIH. If I can understate the case, you can imagine how distressed we are when we hear reports, and we read reports, that the morale is very low at NIH. A lot of good people are leaving. A lot more are going to leave, and so on. Are these reports accurate in your judgment? Have you been there long enough to find out?

Dr. Stone. Some very good people have left. They have gone into highly desirable positions. For example, the new dean of Yale Medical

School and the new dean at Mt. Sinai School of Medicine came from NIH. Dr. Sherman went to a highly responsible position at the AAMC. Those are not mean or small jobs. We are extremely proud that men have gone to positions of that sort. Some other individuals who are leaving or retiring represent the normal rate of attrition at the institutes.

However, I believe there are places where morale, no doubt, could be better. There was a period of uncertainty. My own feeling is that, during the time I have known people on campus, morale has been steadily improving and I hope it will continue to do so.

Mr. Flood. How long have you been out there?

Dr. Stone. Nine months.

Mr. Flood. For what that is worth, what are you doing to improve the situation? When you came in you knew it was a can of worms. You have been there for 9 months, and what are you doing about it?

Dr. Stone. Most of the things I am doing are intangible.

Mr. Flood. Does that help?

Dr. Stone. I believe so.

Mr. Flood. Does it?

Dr. Stone. I believe so. I think talking with people, understanding their fears and anxieties and hopes and ambitions——

Mr. Flood. I misunderstood the word intangible.

Dr. Stone. I meant intangible. They are matters having to do with morale which is, after all, an emotional state. One needs to show by behavior how people can meet their own expectations and I am trying to do that.

Mr. Flood. We are glad to hear you are trying. Of course, we are concerned. Do you have any ideas what this committee can do to help you? What can this committee do to help you?

Dr. Stone. Mr. Flood, your opening statement about the pride that you take in NIH, conveyed to the NIH, will be enormously supportive.

Mr. Flood. I think they have known that for some time.

Dr. Stone. I think it is nice to have it reasserted.

Mr. Flood. That is why I reasserted it. Is that all?

Dr. Stone. That the committee can do?

Mr. Flood. Yes. Have you discussed this with somebody here, there, or someplace? I am going up there on the floor and the other members are going to ask me. Do you have any idea how this committee can help you?

Dr. Stone. Yes, sir. Given the fact that we feel there are resource constraints on us——

RESOURCE CONSTRAINTS

Mr. Flood. There are what?

Dr. Stone. There are resource constraints set at higher levels.

Mr. Flood. Thereby hangs the tale.

Dr. Stone. I think the kind of support you provide by your interest is exactly what we need.

Mr. Flood. But you have not said anything, have you? Is that as far as you are going to go, I suppose?

Dr. Stone. Yes, sir.

STAFFING CUTS

Mr. FLOOD. One of the stories we hear is that the staffing cuts dictated by the OMB more than anything else are producing these morale problems. Have you given any employment ceilings which you are going to require these cutbacks in, in NIH?

Dr. STONE. The present employment ceilings will not require cuts. I have had discussions with the Assistant Secretary and with the Secretary about the hopes we have for an increase in ceilings that will enable us to give support to some Institutes—notably the Heart Institute, which has grown very rapidly and the clinical center where we believe it is appropriate.

Mr. FLOOD. You have not been given any flat ceilings on employment?

Dr. STONE. Yes, of course, we have an employment ceiling.

Mr. FLOOD. I know you have been given employment ceilings. Having been given the employment ceilings, is this what dictates a cutback in NIH without more——

Mr. SCHWARTZ. Yes, sir. During fiscal year 1973, we were at a level of 10,508. Our initial ceiling for fiscal year 1974 was 10,182. It was this cut that started us to do a very thorough investigation of where we had to cut back on staff.

During the development of the fiscal year 1975 budget, we were able to increase this number for fiscal year 1974 to 10,395. At this level we really will not have to make any reduction in force.

Mr. FLOOD. How long have you been around there?

Mr. SCHWARTZ. For 2 years.

Mr. MILLER. Mr. Chairman, may I add a word about the process?

Mr. FLOOD. Yes, sir.

Mr. MILLER. No specific ceiling is given to HEW by OMB by agency. The ceiling we get is two figures: one for social security and one for the rest of HEW. The distribution among agencies is HEW's responsibility. The office of the Secretary allocates a certain amount to the entire health establishment and Dr. Edwards' office divides it among the health agencies. You have the tables before you that show the employment ceiling. The employment increase for HEW is over 2,000 positions for 1975 and Congress itself has voiced dismay over the growth in Federal employment.

Mr. FLOOD. NIH?

Mr. MILLER. No. But you are talking about a limited pie that has to be cut and there are restraints on the total. I do not know whether it has come through clearly. We are intending to increase the ceiling for the NIH above the one originally presented to Congress in the 1974 column in the 1975 budget.

Mr. FLOOD. Suppose you prepare a table showing the actual employment for each one of the Institutes for the past 8 years, along with the estimated employment for fiscal years 1974 and 1975.

Mr. SCHWARTZ. Yes, sir, we will be glad to supply that.

[The information follows:]

10 Year History of NIH Employment

	1965	1966	1967	1968	1969	1970	1971	1972	1973	1974 Est. Original	1974*	1975**
NCI............	1,199	1,252	1,399	1,453	1,411	1,355	1,426	1,665	1,720	1,820	1,820	1,855
NHLI...........	695	589	606	609	564	558	584	618	641	656	687	656
NIDR...........	261	306	280	301	291	283	289	288	287	265	267	265
NIAMDD.........	588	603	616	633	615	588	597	585	579	551	560	551
NINDS..........	678	693	691	732	652	588	583	557	527	515	524	515
NIAID..........	669	716	664	706	695	676	665	623	604	590	599	590
NIGMS..........	147	171	183	207	191	180	164	167	147	153	153	153
NICHD..........	162	299	303	405	400	415	435	482	510	514	523	524
NEI............	--	--	--	--	59	85	92	117	121	127	132	127
NIEHS..........	--	29	63	169	176	202	220	235	228	233	235	233
RR.............	--	--	--	98	85	82	83	78	75	71	71	71
FIC............	--	--	--	62	46	48	47	59	53	49	49	49
Total IRD's..	4,399	4,658	4,805	5,375	5,185	5,060	5,185	5,474	5,492	5,544	5,620	5,519
NLM............	--	--	--	491	489	461	462	465	456	455	465	455
OD.............	--	--	--	--	472	473	489	490	513	525	531	525
MP.............	4,303	4,363	4,188	4,389	3,527	3,403	3,470	3,330	3,326	3,265	3,373	3,284
S&S............	434	462	472	676	779	736	645	624	701	606	605	605
Total, NIH...	9,136	9,483	9,465	10,931	10,452	10,133	10,251	10,383	10,488	10,395	10,595	10,459

*Tentative, pending review by Director, NIH with each Institute Director.

**1975 employment is currently being studied. Final decisions regarding a potential increase in employment ceiling have not yet been made.

TRAINING AND FELLOWSHIP PROGRAM

Mr. FLOOD. One of the major issues in the 1974 budget was this proposed phaseout of training and the fellowship program you are talking about. I take for granted, you know, Doctor, that neither this committee nor the Congress as a whole want any of this proposed phaseout—none. As a matter of fact, this committee added $34,684,000 to the budget for training grants and added $20,491,000 to the budget for the fellowships in order to maintain these programs at the 1972 fiscal level. That shows you that not only the committee but the Congress was pretty clear about it. Under all the circumstances, do you think we made a mistake?

Dr. STONE. I believe the release of those funds demonstrate concurrence with your intentions and wishes and I think is confirmation of the wisdom of what you did.

Mr. FLOOD. I did not hear the first part of your sentence.

Dr. STONE. I said, the release of the funds that were withheld, for me, serves as confirmation of your particular intent. It is an execution of your intent and I think it is confirmation of the good judgment you showed.

Mr. FLOOD. Is this money that we are talking about, that we added, being spent to continue the fellowship and the training program?

Dr. STONE. Yes, sir, with the ground rules somewhat changed. New starts for institutional training grants, as they were formally known, are being funded from 1973 and 1974 funds. The 1975 funds would be used for the development of the new postdoctoral fellowship program.

Mr. FLOOD. Who issued the ground rules after this release you spoke about?

Dr. STONE. The Secretary.

Mr. FLOOD. Did the ground rules come with the release?

Dr. STONE. The Secretary enunciated the ground rules.

Mr. FLOOD. At the time of the release.

Dr. STONE. Yes, sir.

ARTHRITIS TRAINING PROGRAM

Mr. FLOOD. If these funds are being spent for those purposes, why do you think we are receiving complaints like this one?

> As you may already know, despite the intentions of your committee that the National Institutes of Health restore training grant funds in their 1974 budget, the arthritis program is down to 41 trainees this year from 84 in 1972, and by next year the program will be nearly completely phased out as only 4 trainees will remain.

Dr. STONE. Mr. Chairman, I recall that you asked this question when Dr. Edwards was here testifying.

Mr. FLOOD. That is right.

Dr. STONE. And I said I would get additional information. I have that information. The National Institute of Arthritis' estimates for trainees in the field of arthritis, under their training program, are very close to those you quote. Through this mechanism 60 trainees were supported in 1973, 50 will be supported in 1974, and 4 will be supported in 1975. Under the old predoctoral fellowship programs that are also being phased out, support will be provided for 23, 17, and 13 fellows in the years 1973 through 1975. In addition to these, however, under the new post-doctoral fellowship training program, funds are allocated to support 14 research training fellowships in the field of arthritis in 1974 and in 1975 this allocation will be doubled to provide support for 28 fellowships. Thus far only 12 applications for research training fellowships have been received in the area of arthritis. We have a table which displays this and we would be pleased to submit it for the record.

Mr. Flood. Very well.

[The information follows:]

ARTHRITIS TRAINING PROGRAMS

	Fiscal year 1973	Fiscal year 1974	Fiscal year 1975
Trainees (under institutional awards)	60	50	4
Postdoctoral and special fellowships	12	6	4
Research career development awards	10	10	8
Research career awards	1	1	1
Research training fellowships		14	28
Total	83	81	45

TRAINING OF SCIENTISTS

Mr. Flood. Last year in our report in the 1974 appropriation bill, this committee said on page 24 of that report, and let me quote this for you:

> Because research is a creative activity, the sine qua non for its conduct is a competent investigator—a creative scientist may be able to do productive work in inadequate facilities but nothing will result if a few years hence this country is forced to staff its superb facilities with inadequate scientists. It cannot be seriously argued that we have an adequate supply of biomedical investigators and that a moratorium on further training might simply be tried as an experiment until the need for training programs can be more convincingly demonstrated. Not only is the training period required in the medical sciences much too long to risk such a dangerous course, but research scientists are a perishable commodity. With rare exceptions, research is a young person's game and, while it is somewhat less true in the biomedical sciences than in the physical sciences, because of the longer period of training required, the most creative work is usually done in the earlier years of a scientist's career and his most effective role in the later years is as a preceptor, teacher or, perhaps, administrator. It seems very unwise to pursue a course that would have the result, even in a few years, of leaving the entire medical research establishment in the hands of a group of aging scientists past their prime. They will no doubt continue to publish and some useful work would still be done—and we would probably remain comfortably unaware of the more inspired work that was not being done by the bright youngsters who have been denied the opportunity to devote their talents to the fight against disease. The research training and fellowship programs of the NIH are the vehicles for the inescapable competition for brains; the cost of training is simply an investment in the future and the dividends to be reaped—in terms of better health care—are directly dependent on the size of that investment.

That is from the report of the committee.

Dr. Stone. Yes.

Mr. Flood. Interesting?

Dr. Stone. I guess the question is how much Federal support is necessary to fuel that.

Mr. Flood. Do you agree with what we said in the report?

Dr. Stone. I do.

Mr. Flood. You do?

Dr. Stone. Yes; we have got to have the very best minds coming up, being trained, and feeding into the system because certainly there is loss at the other end. Yes, sir. we must continue to foster that in various ways. The question is how much does it need direct Federal support.

Mr. Flood. Did you read this before I just read it to you?

Dr. Stone. Yes.

Mr. Flood. This isn't the first time you heard of that?

Dr. Stone. No, sir.

Mr. Flood. I presume you have talked about it around tables here and there?

Dr. Stone. Yes, we have had discussions.

Mr. Flood. Now I have read this to you and you are here making the presentation for the 1975 budget for NIH as the Director, and I say to you do you agree with what we said in that report, and you say yes, and that is that. Anything else?

Dr. Stone. Under the proposed funding in 1975, we will continue to train young men and women in biomedical research in substantial numbers. The figure I have here is 14,380. I think that is a respectable number.

Mr. Flood. Who is next—me?

Dr. Stone. Yes.

Mr. Flood. I am surprised.

Dr. Stone. Perhaps we can get some more comments. I would like to include Dr. Stetten, Deputy Director for Science and Dr. Kennedy who does planning and evaluation.

Mr. Flood. Good. In view of their titles I would imagine so. I read this thing with some inflection you noticed. I am no amateur at inflection.

Dr. Stone. So I have heard.

Dr. Stetten. I first came to NIH in 1954 and, at that time, my initial assignment in the Arthritis Institute was to do what I could to stem the deteriorating morale as evidenced by the fact that some of the more distinguished scientists in that Institute and other Institutes were leaving. I did what I could. I questioned the ones who were leaving and tried to find out why they were leaving. Of course, the real reason they were leaving was that they were distinguished and therefore being offered attractive jobs on the outside.

This has been a continuing process. It seems to me the departures we have seen in the last year, though they have been hard to take, have not really been more dramatic than departures we have previously seen. This is inevitable in the nature of our Institutes. It is the best, the most renowned, the most productive scientists that receive the most attractive outside offers and therefore leave us.

Mr. Flood. As a matter of fact you were one, weren't you?

Dr. Stetten. Yes; I was one, if you will.

In regard to the mechanism for the support of persons in training, I believe the figures will bear out the fact that it is the intention of the National Institutes of Health to train people in similar numbers to those trained in the past but by a somewhat different vehicle. Instead of giving the support primarily to the institutions and allowing the institutions then to fund the trainees, the bulk of the support, in future years, as envisioned by the Secretary, will be in the form of direct fellowships awarded to the candidates themselves with a modest institutional support attached to each fellowship.

I think the two modes can be debated; each has advantages and each has disadvantages.

Mr. Flood. When I read you the quotation from last year's report and you finally said yes, if you agree, why does the 1975 budget again propose to phase out the training grant program? All of those things being true, why?

Dr. Stone. It continues the phase-out of the old programs. There will be some instances in which institutions are supported in shortage areas—where we believe that the only way to overcome the shortage is to provide an additional incentive to the institutions to provide the milieu in which the training can occur. There will be some such support, therefore. We do not propose to phase it out. We are changing the emphasis, the balance, as it were.

Mr. Flood. You say with the new program no training for clinical practice as a so-called specialty training will be permitted?

Dr. Stone. Yes.

CLINICAL TRAINING CURRENTLY SUPPORTED

Mr. Flood. How much training of this type is NIH currently supporting? You ought to have some figures on that.

Mr. Schwartz. For fiscal year 1974 there will be 75 awards at a cost of $6,840,000. For fiscal year 1975 it will be 45 awards at a cost of $2,400,000.

Mr. Flood. Is it really possible to distinguish between training for clinical practice and training for research? How do you do that—with mirrors?

Dr. Kennedy. It is extraordinarily difficult because in the clinical sciences physicians who are seeking subspecialty training frequently engage in much the same sort of enterprise as people who aspire to long-term research careers, and both are in the process conducting research and advancing the field.

What we intend is that only those physicians who aspire to research careers will be the recipients of research training support, and that physicians whose avowed career aspiration is to take care of sick people will not receive research training support. We feel there are alternative sources of support for training for service.

Mr. Flood. Even so, Doctor, tell us the reasons why you think this committee should agree to your proposals. Give me 11 reasons.

Dr. Stone. By giving the money directly to the individuals we are increasing the number of individuals whom we can support. We also give those individuals a greater degree of autonomy in the selection of their training sites. And the administration's philosophy is that it is a healthy approach to give the individual responsibility for his own development.

It has sometimes been said that some of the institutional support was, perhaps, not used as directly as one might hope in support of the training program. We believe we can get the most mileage for the dollar by the present proposal.

We believe there will be an opportunity to focus more sharply in the shortage areas in the preparation of research fellows, that is, by designating the shortage areas to the extent it has been possible to do so.

Each Institute has been polled and the Institute director and the staff and their external advisers have proposed areas in which they perceive a real need for further research fellowship support. Instead of having a rather broadcast program we can decide what areas need support and push those.

Mr. FLOOD. Needless to say we are confused by figures. Take a look at page 10 and 11 of your statement with respect to fellowship and training grants.

Suppose you supply for the record another table. This table will be for each Institute—number of fellowships, dollar amounts for academic years 1971 through 1975, and also identify the fiscal year for which the funds are appropriated. And also give us the same information for the training grants. That is a little complicated. Work the format on that out with Mr. Neil.

[The information follows:]

NATIONAL INSTITUTES OF HEALTH

FELLOWSHIPS AND TRAINING GRANTS

[Amounts in thousands of dollars]

	1971		1972		1973		1974		1975	
	Number	Amount	Number	Amount	Number	Amount	Number	Amount	Number	Amount
Fellowships:										
Noncompeting	1,213	8,663	767	5,648	723	6,108	523	5,433	2,408	34,017
Competing	157	1,430	111	1,074	53	634	14	225	20	260
New	1,144	11,179	1,226	12,656	1,054	12,791	2,239	34,359	1,798	26,828
Supplemental	(49)	29	(44)	38	(73)	78	(2)	150	--------	50
Total	2,514	21,301	2,104	19,416	1,830	19,611	2,776	40,167	4,226	61,155

	1971		1972		1973		1974		1975	
	FTE	Amount	FTE	Amount	FTE	Amount	FTE	Amount	FTE	Amount
Training grants:										
Noncompeting	8,499	102,155	9,197	108,774	8,065	95,376	7,734	93,737	7,517	61,244
Competing	1,789	22,903	1,886	23,329	1,730	22,463	183	2,533	--------	--------
New	496	6,408	508	6,670	511	7,223	40	792	--------	--------
Supplemental	108	1,843	59	1,663	3,103	24,106	55	753	50	600
Total	10,892	133,309	11,650	140,436	13,409	149,168	8,012	97,815	7,567	61,844

	Number in training by academic year				
	1970–71	1971–72	1972–73	1973–74	1974–75
Fellowships:					
Noncompeting	1,155	804	750	586	1,136
Competing	148	126	84	35	7
New	1,007	1,152	958	1,067	2,338
Supplemental	(62)	(101)	(52)	(4)	(35)
Total	2,310	2,082	1,792	1,688	3,481
Training grants:					
Noncompeting	10,516	10,063	10,382	8,248	8,765
Competing	1,910	2,275	2,040	1,558	488
New	600	701	447	415	209
Supplemental	85	23	69	284	2,810
Total	13,111	13,062	12,938	10,505	12,272

NATIONAL CANCER INSTITUTE—FELLOWSHIPS AND TRAINING GRANTS

[Amounts in thousands of dollars]

	1971		1972		1973		1974		1975	
	Number	Amount	Number	Amount	Number	Amount	Number	Amount	Number	Amount
Fellowships:										
Noncompeting	44	474	15	136	30	314	42	454	394	5,516
Competing	21	141	19	193	14	136				
New	126	1,171	163	1,592	157	1,719	390	5,450	536	6,550
Supplemental										
Total	191	1,736	197	1,921	201	2,169	432	5,904	930	12,066

	1971		1972		1973		1974		1975	
	FTE	Amount	FTE	Amount	FTE	Amount	FTE	Amount	FTE	Amount
Training grants:										
Noncompeting	623	8,332	847	10,894	810	10,100	909	12,259	423	6,097
Competing	151	2,134	298	4,335	150	2,713				
New	24	222	100	1,084	74	930				
Supplemental	5	86	13	161	198	3,456				
Total	803	10,774	1,258	16,474	1,232	17,199	909	12,259	423	6,097

Number in training by academic year

	1970–71	1971–72	1972–73	1973–74	1974–75
Fellowships:					
Noncompeting	97	44	15	30	42
Competing	9	21	19	14	
New	65	126	163	157	390
Supplemental					
Total	171	191	197	201	432
Training grants:					
Noncompeting	787	938	1,215	859	964
Competing	366	228	225	159	
New	82	36		78	
Supplemental	20	8	6	212	
Total	1,255	1,210	1,446	1,308	964

NATIONAL HEART AND LUNG INSTITUTE—FELLOWSHIPS AND TRAINING GRANTS

[Amounts in thousands of dollars]

	1971		1972		1973		1974		1975	
	Number	Amount	Number	Amount	Number	Amount	Number	Amount	Number	Amount
Fellowships:										
Noncompeting	57	617	28	249	43	401	32	316	400	5,685
Competing	9	110	11	85	1	20				
New	95	1,140	105	977	56	775	368	5,500	260	5,000
Supplemental		9								
Total	161	1,876	144	1,311	100	1,196	400	5,816	660	10,685
	1971		1972		1973		1974		1975	
	FTE	Amount	FTE	Amount	FTE	Amount	FTE	Amount	FTE	Amount
Training grants:										
Noncompeting	780	13,405	776	14,330	712	14,000	450	8,100	150	2,000
Competing	148	2,879	124	2,842	188	3,207				
New	84	1,081	76	1,261	80	1,179				
Supplemental		252		121		276				
Total	1,012	17,617	976	18,554	980	18,662	450	8,100	150	2,000

	Number in training by academic year				
	1970–71	1971–72	1972–73	1973–74	1974–75
Fellowships:					
Noncompeting	57	28	43	32	400
Competing	9	11	1	0	0
New	95	105	56	368	260
Supplemental	0	0	0	0	0
Total	161	144	100	400	660
Training grants:					
Noncompeting	1,122	1,170	1,164	1,068	675
Competing	252	222	186	282	0
New	96	126	114	120	0
Supplemental	0	0	0	0	0
Total	1,470	1,518	1,464	1,470	675

NATIONAL INSTITUTE OF DENTAL RESEARCH—FELLOWSHIPS AND TRAINING GRANTS

[Amounts in thousands of dollars]

	1971		1972		1973		1974		1975	
	Number	Amount	Number	Amount	Number	Amount	Number	Amount	Number	Amount
Fellowships:										
Noncompeting	31	288	33	410	34	572	18	220	140	2,300
Competing	6	109	6	124	6	164	4	120		
New	21	289	28	388	26	444	140	2,460	40	600
Supplemental	(3)	3	(1)	6	(1)	6	(2)	100		
Total	58	689	67	928	66	1,186	162	2,900	180	2,900

	1971		1972		1973		1974		1975	
	FTE	Amount	FTE	Amount	FTE	Amount	FTE	Amount	FTE	Amount
Training grants:										
Noncompeting	390	4,967	321	4,393	261	3,670	185	2,477	205	2,785
Competing	10	158	53	474	105	1,185	20	308		
New	12	299	28	415	19	280				
Supplemental	1	27	7	300	3	135	50	600	50	600
Total	413	5,451	409	5,582	388	5,270	255	3,385	255	3,385

	Number in training by academic year				
	1970–71	1971–72	1972–73	1973–74	1974–75
Fellowships:					
Noncompeting	35	30	34	18	195
Competing	2	1	1	4	
New	31	33	3	140	40
Supplemental				(2)	
Total	68	64	38	162	235
Training grants:					
Noncompeting	387	390	318	222	220
Competing	16	10	72	56	
New	5	2	14		
Supplemental	4	1		31	35
Total	412	403	404	309	255

NATIONAL INSTITUTE OF ARTHRITIS, METABOLISM, AND DIGESTIVE DISEASES—FELLOWSHIPS AND TRAINING GRANTS

[Amounts in thousands of dollars]

	1971		1972		1973		1974		1975	
	Number	Amount	Number	Amount	Number	Amount	Number	Amount	Number	Amount
Fellowships:										
Noncompeting	83	783	63	569	72	611	56	500	155	2,023
Competing	16	162	15	156	12	118	6	52		
New	123	1,360	137	1,356	110	1,089	209	2,430	160	2,000
Supplemental										
Total	222	2,305	215	2,081	194	1,818	271	2,982	315	4,023

	1971		1972		1973		1974		1975	
	FTE	Amount	FTE	Amount	FTE	Amount	FTE	Amount	FTE	Amount
Training grants:										
Noncompeting	568	11,898	578	12,523	427	10,441	442	11,696	116	1,506
Competing	102	2,277	99	2,014	83	2,017				
New	55	778	28	397	114	2,440				
Supplemental		119		138		174				
Total	725	15,072	705	15,072	624	15,072	442	11,696	116	1,506

	Number in training, by academic year				
	1970–71	1971–72	1972–73	1973–74	1974–75
Fellowships:					
Noncompeting	71	73	70	65	172
Competing	16	15	14	9	4
New	112	114	112	171	181
Supplemental					
Total	199	202	196	245	357
Training grants:					
Noncompeting	678	617	628	461	446
Competing	101	111	108	89	
New	25	60	29	124	
Supplemental					
Total	804	788	765	674	446

BUDGET AUTHORITY—NATIONAL INSTITUTES OF HEALTH

NATIONAL INSTITUTE OF NEUROLOGICAL DISEASES AND STROKE—FELLOWSHIPS AND TRAINING GRANTS

[Dollar amounts in thousands]

	1971		1972		1973		1974		1975	
	Number	Amount	Number	Amount	Number	Amount	Number	Amount	Number	Amount
Fellowships:										
Noncompeting			20	135	31	277	18	221	201	3,009
Competing	36	270	27	214	3	25				
New	67	492	69	674	28	247	200	3,000	29	432
Supplemental	(14)	5	(9)	4	(25)	10				
Total	103	767	116	1,027	62	559	218	3,221	230	3,441

	1971		1972		1973		1974		1975	
	FTE	Amount	FTE	Amount	FTE	Amount	FTE	Amount	FTE	Amount
Training grants:										
Noncompeting	534	8,575	565	9,116	652	12,260	717	7,267	300	3,715
Competing	330	3,959	298	3,596	111	1,742	43	685		
New	120	1,514	87	1,381	40	774				
Supplemental	6	252	6	192	104	2,384	2	48		
Total	990	14,300	956	14,285	907	17,160	726	8,000	300	3,715

	Number in training, by academic year				
	1970–71	1971–72	1972–73	1973–74	1974–75
Fellowships:					
Noncompeting			20	31	18
Competing	43	36	27	3	
New	46	67	69	24	204
Supplemental					
Total	89	103	116	58	222
Training grants:					
Noncompeting	744	587	621	717	789
Competing	169	363	328	122	47
New	168	132	96	30	14
Supplemental	29	6	6	5	2
Total	1,110	1,088	1,051	874	852

NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES—FELLOWSHIPS AND TRAINING GRANTS

[Dollar amounts in thousands]

BUDGET AUTHORITY COMPARABLE

	1971		1972		1973		1974		1975	
	Number	Amount	Number	Amount	Number	Amount	Number	Amount	Number	Amount
Fellowships:										
Noncompeting	69	643	65	650	27	232	12	95	122	1,899
Competing	4	36	2	20						
New	23	207	28	262	121	1,338	103	2,374	137	2,760
Supplemental		2								
Total	96	888	95	932	148	1,570	115	2,469	259	4,659

	1971		1972		1973		1974		1975	
	FTE	Amount	FTE	Amount	FTE	Amount	FTE	Amount	FTE	Amount
Training grants:										
Noncompeting	762	7,018	720	7,311	750	6,224	474	4,524	336	4,301
Competing	90	1,090	72	902	42	262				
New	54	486	84	617	18	98				
Supplemental	96	198	18	92	268	2,399				
Total	1,002	8,792	894	8,922	1,078	8,983	474	4,524	336	4,301

	Number in training by academic year				
	1970–71	1971–72	1972–73	1973–74	1974–75
Fellowships:					
Noncompeting	62	25	44	27	11
Competing	4	4	3		
New	62	67	49	14	113
Supplemental					
Total	128	96	96	41	124
Training grants:					
Noncompeting	804	840	790	900	494
Competing	156	90	72	6	42
New	84	54	84	12	24
Supplemental			32	6	256
Total	1,044	984	978	924	816

NATIONAL INSTITUTES OF HEALTH

NATIONAL INSTITUTE OF GENERAL MEDICAL SCIENCES—FELLOWSHIPS AND TRAINING GRANTS

[Amounts in thousands of dollars]

	1971		1972		1973		1974		1975	
	Number	Amount	Number	Amount	Number	Amount	Number	Amount	Number	Amount
Fellowships:										
Noncompeting	816	4,980	446	2,655	360	2,515	243	2,429	624	8,277
Competing	54	466	19	172	13	134	3	35	20	260
New	488	4,247	414	4,131	322	4,361	482	7,300	321	4,931
Supplemental			(------)		(------)	49	(------)	50	(------)	50
Total	1,358	9,693	879	6,958	695	7,059	728	9,814	965	13,518

	1971		1972		1973		1974		1975	
	FTE	Amount	FTE	Amount	FTE	Amount	FTE	Amount	FTE	Amount
Training grants:										
Noncompeting	3,594	35,337	4,320	37,628	3,260	24,540	3,830	37,248	5,184	30,349
Competing	693	7,152	650	5,760	772	8,368				
New	73	1,042	30	238	58	668				
Supplemental		215		120	2,413	13,935	1	37		
Total	4,360	43,746	5,000	43,746	6,503	47,511	3,831	37,285	5,184	30,349

	Number in training by academic year				
	1970–71	1971–72	1972–73	1973–74	1974–75
Fellowships:					
Noncompeting	713	515	353	264	103
Competing	53	23	17	3	
New	410	377	270	25	665
Supplementals	(62)	(101)	(52)	(2)	(35)
Total	1,176	915	640	292	768
Training grants:					
Noncompeting	4,543	4,125	4,421	2,957	4,133
Competing	684	920	726	764	8
New	69	205	31	16	42
Supplementals	5	8	6	10	2,404
Total	5,301	5,258	5,184	3,747	6,587

NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT—FELLOWSHIPS AND TRAINING GRANTS

[Amounts in thousands of dollars]

	1971		1972		1973		1974		1975	
	Number	Amount	Number	Amount	Number	Amount	Number	Amount	Number	Amount
Fellowships:										
Noncompeting	43	380	31	297	34	341	20	280	194	2,616
Competing	4	48	1	13	3	26	1	18		
New	53	486	57	555	75	738	155	2,444	153	2,065
Supplemental										
Total	100	914	89	865	112	1,105	176	2,742	347	4,681
	1971		1972		1973		1974		1975	
	FTE	Amount	FTE	Amount	FTE	Amount	FTE	Amount	FTE	Amount
Training grants:										
Noncompeting	754	7,293	684	7,555	792	8,559	374	4,400	630	6,993
Competing	168	1,793	172	1,724	231	2,289	120	1,540		
New	38	422	36	409	92	612	21	384		
Supplemental		634		454		138				
Total	960	10,142	892	10,142	1,115	11,598	515	6,324	630	6,993

	Number in training by academic year				
	1970–71	1971–72	1972–73	1973–74	1974–75
Fellowships:					
Noncompeting	52	43	31	34	20
Competing	3	4	1	1	3
New	31	53	57	9	221
Supplemental					
Total	86	100	89	44	244
Training grants:					
Noncompeting	968	942	855	723	729
Competing	123	223	215	50	386
New	62	42	45	17	122
Supplemental					
Total	1,153	1,207	1,115	790	1,237

NATIONAL EYE INSTITUTE—FELLOWSHIPS AND TRAINING GRANTS

[Amounts in thousands of dollars]

	1971		1972		1973		1974		1975	
	Number	Amount	Number	Amount	Number	Amount	Number	Amount	Number	Amount
Fellowships:										
Noncompeting	4	33	1	15	40	428	30	403	123	1,882
Competing	6	75	10	85		5				
New	55	789	96	1,197	52	825	81	1,249	53	771
Supplemental										
Total	65	897	107	1,297	92	1,258	111	1,652	176	2,653

	1971		1972		1973		1974		1975	
	FTE	Amount	FTE	Amount	FTE	Amount	FTE	Amount	FTE	Amount
Training grants:										
Noncompeting	105	2,667	77	2,174	113	3,055	83	2,495	75	1,994
Competing	5	331	25	573	15	343				
New			13	251			19	408		
Supplemental										
Total	110	2,998	115	2,998	128	3,398	102	2,903	75	1,994

	Number in training by academic year				
	1970–71	1971–72	1972–73	1973–94	1974–75
Fellowships:					
Noncompeting	4	1	40	30	123
Competing	6	10			
New	55	96	52	81	53
Supplemental					
Total	65	107	92	111	176
Training grants:					
Noncompeting	42	31	43	33	30
Competing	6	10			
New		5	8	8	
Supplemental					
Total	48	46	51	41	30

NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES—FELLOWSHIPS AND TRAINING GRANTS

[Amounts in thousands of dollars]

	1971		1972		1973		1974		1975	
	Number	Amount	Number	Amount	Number	Amount	Number	Amount	Number	Amount
Fellowships:										
Noncompeting	8	84	9	70		5	3	31	39	593
Competing										
New	4	30	3	24	5	37	37	560	33	482
Supplemental										
Total	12	114	12	94	5	42	40	591	72	1,075

	1971		1972		1973		1974		1975	
	FTE	Amount	FTE	Amount	FTE	Amount	FTE	Amount	FTE	Amount
Training grants:										
Noncompeting	272	1,969	191	2,141	189	1,688	203	2,195	48	700
Competing	50	646	81	900	27	255				
New	35	442			6	60				
Supplemental		60	15	66	117	1,194				
Total	357	3,117	287	3,107	339	3,197	203	2,195	48	700

	Number in training by academic year				
	1970–71	1971–72	1972–73	1973–74	1974–75
Fellowships:					
Noncompeting	7	8	9		3
Competing					
New	8	4	3	3	39
Supplemental					
Total	15	12	12	3	42
Training grants:					
Noncompeting	338	302	212	209	226
Competing	22	56	90	26	5
New		39			7
Supplemental	27		17	18	111
Total	387	397	319	253	349

DIVISION OF RESEARCH RESOURCES—FELLOWSHIPS AND TRAINING GRANTS

[Amounts in thousands of dollars]

	1971		1972		1973		1974		1975	
	Number	Amount	Number	Amount	Number	Amount	Number	Amount	Number	Amount
Fellowships:										
Noncompeting	7	80	6	66	1	5	6	57	16	217
Competing	1	13	1	12	1	6				
New	4	33	5	47	2	21	17	234	3	42
Supplemental										
Total	12	126	12	125	4	32	23	291	19	259

	1971		1972		1973		1974		1975	
	FTE	Amount	FTE	Amount	FTE	Amount	FTE	Amount	FTE	Amount
Training grants:										
Noncompeting	26	352	18	183	16	178	19	369	5	75
Competing			8	150	6	82				
New										
Supplemental				19		15	2	68		
Total	26	352	26	352	22	275	21	437	5	75

	Number in training by academic year				
	1970–71	1971–72	1972–73	1973–74	1974–75
Fellowships:					
Noncompeting	5	7	6	1	6
Competing	3	1	1	1	
New	5	4	5	2	17
Supplemental					
Total	13	12	12	4	23
Training grants:					
Noncompeting	30	30	15	16	19
Competing			12	4	
New					
Supplemental			2	2	2
Total	30	30	29	22	21

FOGARTY INTERNATIONAL CENTER—FELLOWSHIPS

[Amounts in thousands of dollars]

	1971		1972		1973		1974		1975	
	Number	Amount	Number	Amount	Number	Amount	Number	Amount	Number	Amount
Fellowships:										
Noncompeting	51	301	50	396	51	407	43	427		
New	85	935	121	1,453	100	1,197	57	1,358	73	1,195
Supplemental	(32)	10	(34)	28	(47)	13				
Total	136	1,246	171	1,877	151	1,617	100	1,785	73	1,195

	Number in training by academic year				
	1970–71	1971–72	1972–73	1973–74	1974–75
Fellowships:					
Noncompeting	52	30	85	54	43
Competing					
New	87	106	119	73	155
Supplemental					
Total	139	136	204	127	198

NATIONAL LIBRARY OF MEDICINE—TRAINING GRANTS

[Amounts in thousands of dollars]

	1971		1972		1973		1974		1975	
	FTE	Amount	FTE	Amount	FTE	Amount	FTE	Amount	FTE	Amount
Training grants:										
Noncompeting	91	342	100	526	83	661	48	707	45	729
Competing	42	484	6	59						
New	1	122	26	617	10	182				
Supplemental										
Total	134	948	132	1,202	93	843	48	707	45	729

	Number in training by academic year				
	1970–71	1971–72	1972–73	1973–74	1974–75
Training grants:					
Noncompeting	73	91	100	83	40
Competing	15	42	6		
New	9		26	10	
Supplemental					
Total	97	133	132	93	40

CANCER AND HEART AND LUNG INSTITUTE

Mr. Flood. That 1975 budget again proposes increases for Cancer and Heart and Lung Institutes and decreases or has level funding, keeping in mind inflation, for the rest of NIH. Does this allocation of resources really make any sense after what you said?

Dr. Stone. It is a reflection of both administration and congressionally mandated emphasis in biomedical research. We believe, within the resources available to us, that is a reasonable distribution.

ALLOCATION OF RESOURCES

Mr. Flood. Within the total NIH budget, $1.8 billion, do you think the present allocation of the funds among the Institutes is about right or would you cut that pie Mr. Miller was talking about up a little differently? There is an invitation.

Dr. Stone. I have some preferences on the basis of broad scale programs. I have some personal interest in child health and human development and in environment. I know those are not oriented toward specific diseases, but I think, in many ways, that is the state of our needs.

Mr. Flood. I am talking to you.

Dr. Stone. I am responding. I say I think broad-based programs such as child health, human development, environmental health sciences are areas that ought to be heavily supported by the administration and by the Congress because they affect our health generally and they affect how human beings grow and what they become. I would like to see emphasis put there rather than in narrow, selective disease areas.

GENERAL RESEARCH SUPPORT GRANTS

Mr. Flood. We are having difficulty understanding the reason for this proposed termination of general research support grants.

Dr. Stone. Yes, sir.

Mr. Flood. Tell us why you think the committee should agree with that proposal.

Dr. Stone. That represents a difficult judgmental decision on our part. I have outlined some of the reasons why that seemed to us justified—that the institutions, which were growing and formerly had rather slender support for providing the mileu for research careers, have now grown enormously. They have capabilities that were not thought of at the time the GRSG was first started. I think those institutions are now capable of providing a proper environment without this support.

Again, given a limitation on the total amount of dollars available, we would rather take the money and use it for selective programs than use it in a kind of undifferentiated way. We think we can get more mileage for the dollars by putting them into individual institutes and allocating them to specific programs. It is a matter of judgment, not absolute.

DIRECTED RESEARCH

Mr. Flood. The termination of the general support grant seems to be clearly inconsistent with the Administration's philosophy that recipients of Federal funds should have more discretion as to how they are used and there should be less direction from Washington, big brother and so on. How do you explain this increasing emphasis on directed research as opposed to the investigation or initiated research?

Dr. Stone. I think the discretion that is exercised by individual scientists must be preserved. We can make resource allocation at the level of saying that we are going to put so many millions of dollars into diabetes research or hypertension or sudden infant death syndrome but we should not attempt to be more directive than that.

Mr. Flood. Aren't you placing emphasis on directed research?

Dr. Stone. Yes, sir. To the extent that we will put so many million dollars into diabetes and so forth—we believe that research then should be led and driven by the ingenuity and the ideas of the individual scientist. But at some level there has to be some targeting. The entire NIH budget, as I said earlier, represents targeting from the congressional point of view. You say that a particular amount of money ought to be spent on health research and that is targeting. Then our responsibility is to do it—without getting so precise that it becomes too restrictive or that the scientist is constrained in developing his ideas. We think there should be some further allocation of resources. We attempt to make the proper allocation of resources both with internal and external advice.

Mr. FLOOD. One of your predecessors, Dr. Shannon, thought the key to progress in medical research was the creation of strong research institutions all throughout the Nation.

Dr. STONE. Yes.

GENERAL RESEARCH SUPPORT GRANTS

Mr. FLOOD. If you withdraw these general support grants, will that weaken the institutions which had been receiving them?

Dr. STONE. The money will still be available to them. It will simply come under some broad designation such as research in diabetes or research in hypertension or research in renal disease.

Mr. FLOOD. What about the money to the institutions? Are you going to weaken them?

Dr. STONE. Institutions still receive the indirect costs of providing the research environment as part of regular research grants programs. That is still available to them, and that has been steadily increasing over the last half dozen years. We have figures to show how enormously that indirect support for research has increased. We believe that is a substantial measure of substitution for general institutional support.

Mr. FLOOD. There won't be a withdrawal of general research support grants?

Dr. STONE. I say it will distributed differently. The funds will be in individual Institutes and in individual programs, but the money hasn't disappeared. It is simply no longer under the rubric of GRS.

APPEALS BOARD

Mr. FLOOD. When Dr. Edwards was here I discussed with him the idea of creating an appeals board. We spent some time on that. This would be made up of people who could review objectively cases where investigators with a little offbeat ideas have been turned down by the study sections, the advisory committees made up of the so-called in group in a particular field.

We have the uneasy feeling that we may be overlooking some brilliant discovery just because it is not in the mainstream or because the person proposing it does not have the proper long hair, academic credentials or something. This could happen. I asked him about it and I ask you about it. Will you look into that?

Dr. STONE. Might I take advantage of Dr. Stetten's presence? He is a notable scientist and I would like to have his reaction.

Dr. STETTEN. I have no doubt that any system that could be devised could fail to detect an unsung genius. This is always possible. I believe the system which we actually use is designed to catch most of such people and fund them if they are really good.

The reason is that our study sections are large. They run an average of about 15 persons coming from different campuses. There are usually one or more persons in each study section who will be sensitive to the peculiar genius of the unusual application and will rise to its defense.

Mr. Flood. I like this idea of an appeals board, out of an abundance of caution, if for no other reason.

Dr. Stone. We often have "ad hoc" committees. Just today I had a note on my desk concerning an inquiry about a man in a Federal lab with quite an unconventional idea about how cancer develops. The Cancer Institute had first put his work through the routine and then afterward appointed a special ad hoc committee that went out and made a site visit. We do this sort of thing very frequently.

Can you describe that visit, leaving out the names, Dr. Rauscher?

Dr. Rauscher. There is an appeals board, in effect, in the form of the Advisory Board. If any member of the Board, or a member of the relevant study section feels that a disservice has been done in the evaluation of the proposal, we take it to our Board and recommend to them that a special study section be set up or that the original study section rereview that application.

We have had something like 20 of these just in the past 3-month period. Some of those are now being reviewed and will be brought up for re-presentation to the Cancer Board when they meet again in June.

So, in effect, we are talking about a 3-month delay. That is a lot of time, but I think the system can work and it does. It is not infallible.

Dr. Stone. When I was at the Rockefeller University, I was told a story about Dr. Shope, who was one of the very important early biomedical men in this country. He was interested in the cure of cancer, and he was sent a shipment of sassafras roots by a man in Texas who claimed he brewed it up and cured his own cancer. Dr. Shope, in spite of the fact he was an eminent scientist, smelled up the Rockefeller University with sassafras roots trying to test the man's proposal, even though he thought it had no merit. That sort of thing goes on fairly routinely in science. Cancer is a field that attracts some people with very eccentric ideas sometimes.

Memorial Hospital is presently trying out some drugs that had gotten rather poor reviews and is giving them very careful testing.

The process, I believe, has some safeguards but the public must, of course, be protected from those who are either deluded or outright quacks. We try to do that. We try to make a balance.

MULTIYEAR GRANTS

Mr. Flood. It is reported that you are funding some of these projects for 2 years instead of 1 year at a time like the practice in the past. Is there anything to these stories?

Dr. Stone. Yes, that is true.

Mr. Flood. Tell us about the multiyear funding business.

Dr. Stone. I would like Mr. Schwartz to describe it specifically.

Mr. Schwartz. All impounded funds released from fiscal year 1973 are being awarded in the normal fashion in which those funds would have been awarded; that is, primarily in single year grants. There are a number of awards that in prior years have been awarded on a multiyear basis, and in those cases they will continue to be awarded in that fashion for fiscal year 1973.

For fiscal year 1974, there will be something in the order of $100 million that will be put out in multiyear grants. Therefore, $50 million will be utilized in fiscal year 1974 for prepayment of fiscal year 1975 awards.

The reason for doing this is that 7 months of the fiscal year had elapsed before we were in a position to know the full extent of our resources——

Mr. FLOOD. How long have you been doing this 2-year business?

Mr. SCHWARTZ. In some cases, it has been relatively small amounts from year to year that have been put into 2-year awards.

This year it is an unusually large amount because, with only 5 months left in the fiscal year, we received something in the order of $450 million over and above our current programing——

Mr. FLOOD. Hasn't the practice in the past been 1 year at a time?

Mr. SCHWARTZ. Largely it has been 1 year.

Mr. FLOOD. It has been?

Mr. SCHWARTZ. That is correct.

Mr. FLOOD. When did you start this is what I am trying to find out? And to what extent are you doing it?

Mr. SCHWARTZ. This is the first fiscal year it has been done to any large extent.

Mr. FLOOD. This is the first time you have done this?

Mr. SCHWARTZ. That is correct, but this was a very unusual year in the amount of funds that were available.

Mr. FLOOD. It is a very unusual year—period.

Mr. MILLER. I think Mr. Schwartz gave the key answer to you, but I——

Mr. FLOOD. What was that?

Mr. MILLER. I refer to his point that it is late in the fiscal year, and in order to spend the funds appropriately it is much better to "multiyear fund." This is an unusual year, and we can't drop it at that. The increased funding that was created by releasing 1973 funds and also spending the 1974 congressional increases created a 1-year very high level of funding. If we planned to make only 1-year awards in all cases, the demand on the 1975 resources would have been beyond our capacities to handle within the budget. So it was indeed a most unusual year.

Mr. FLOOD. It just never happened before.

Mr. MILLER. We never had a year like this in the creation of such a high spending level.

Mr. SCHWARTZ. I might add, Mr. Flood, that we could have funded all of these projects in fiscal year 1975 but it would have seriously reduced the amounts available for new projects. There was a tradeoff we had to make to get a good balance between continuation support of 1974 projects and our ability to start new projects during the next fiscal year.

NEW INSTITUTE DIRECTORS

Mr. FLOOD. I want something for the record here.

How many new institute directors have been appointed in the past year, a list of them, names, addresses, and so on.

[The information follows:]

NEW DIRECTORS APPOINTED

There have been no new institute directors appointed within the past year.

INSTITUTES WITHOUT DIRECTORS

Mr. FLOOD. How many institutes have no directors or acting directors at the present time, a list of them.

[The information follows:]

ACTING DIRECTORS

The institutes listed below have acting directors, at the present time:

National Institute of Neurological Diseases and Stroke, Dr. Donald B. Tower, appointed May 1, 1973.

National Institute of General Medical Sciences, Dr. Leo H. von Euler, appointed February 1974.

National Institute of Child Health and Human Development, Dr. Gilbert L. Woodside, appointed September 1973.

COMPETING AND NONCOMPETING GRANTS

Mr. FLOOD. Tables for the record summarizing by institutes the dollar amounts for competing and noncompeting research grants for fiscal years 1973, 1974, and 1975.

[The information follows:]

DHEW - National Institutes of Health

REGULAR RESEARCH GRANTS

Funded - Unfunded
(Amounts in thousands)

	1971		1972		1973		1974		1975	
	No.	Amount	No.	Amount	No.	Amount	No.	Amount	No.	Amount
NCI:										
Funded	979	$49,567	1282	$69,309	1514	$86,203	1719	$115,153	1773	$115,140
Non-competing	594	31,681	694	36,417	1013	54,688	1030	64,532	1240	74,512
Competing	385	17,886	588	32,892	501	31,515	689	50,621	533	40,628
Renewals	173	9,264	204	13,346	129	10,365	243	16,852	208	16,837
New	212	7,223	384	17,122	372	18,085	446	29,567	325	20,265
Supplementals	(130)	1,399	(127)	2,424	(161)	3,065	(234)	4,202	(135)	3,526
Percent funded:										
Competing	59%		66%		55%		54%		36%	
Total	78		81		79		75		65	
Unfunded	269	14,151	308	12,458	403	18,707	579	26,543	956	48,167
Renewals	96	5,590	80	3,487	60	2,998	94	6,439	234	14,387
New	173	8,561	228	8,971	343	15,709	485	20,104	722	33,780
NHLI:										
Funded	1481	104,065	1457	123,419	1375	132,789	1568	155,479	1767	171,653
Non-competing	1026	62,165	975	81,139	983	96,473	996	111,538	1156	129,761
Competing	455	41,900	482	42,280	392	36,316	572	43,941	611	41,892
Renewals	211	14,084	220	16,435	182	17,470	172	16,727	200	11,778
New	244	25,924	262	22,989	210	15,536	400	23,848	411	27,614
Supplementals	(173)	1,892	(138)	2,856	(199)	3,310	(138)	3,366	(125)	2,500
Percent funded:										
Competing	65%		64%		44%		46%		47%	
Total	86		84		74		70		72	
Unfunded	242	15,958	268	12,159	494	22,222	682	34,469	702	51,500
Renewals	89	8,705	88	4,993	157	8,219	184	10,091	180	10,200
New	153	7,253	180	7,166	337	14,003	498	24,378	522	41,300
NIDR:										
Funded	211	10,751	253	13,837	272	14,666	243	15,658	213	12,646
Non-competing	116	6,684	142	8,407	199	11,506	170	9,599	178	11,000
Competing	95	4,067	111	5,430	73	3,160	73	6,059	35	1,646
Renewals	32	2,490	39	2,857	30	1,679	23	3,432	24	1,146
New	63	1,519	72	2,461	43	1,227	50	2,407	11	500
Supplementals	(8)	58	(11)	112	(5)	254	(6)	220	--	--
Percent funded:										
Competing	44%		54%		38%		36%		16%	
Total	63		73		70		65		54	
Unfunded	122	4,255	94	2,942	118	4,949	130	6,618	178	9,252
Renewals	16	1,037	17	963	22	1,433	26	1,690	27	1,755
New	106	3,218	77	1,979	96	3,516	104	4,928	151	7,497
NIAMDD:										
Funded	1880	80,735	1854	93,593	1647	91,292	1833	113,037	1642	102,996
Non-competing	1450	61,473	1237	62,638	1322	68,331	1135	67,838	1153	69,080
Competing	430	19,262	617	30,955	325	22,961	698	45,199	489	33,916
Renewals	247	11,564	340	18,352	201	14,688	476	25,885	277	18,250
New	183	6,598	277	10,819	124	6,499	222	18,914	212	15,166
Supplementals	(139)	1,100	(186)	1,784	(133)	1,774	(34)	400	(42)	500
Percent funded:										
Competing	47%		55%		32%		46%		38%	
Total	79		79		70		69		67	
Unfunded	493	25,385	502	22,876	705	32,827	825	47,117	811	51,139
Renewals	221	13,624	209	10,762	329	13,109	389	19,380	415	23,125
New	272	11,761	293	12,114	376	19,718	436	27,737	396	28,014

(Amounts in thousands)

	1971		1972		1973		1974		1975	
	No.	Amount	No.	Amount	No.	Amount	No.	Amount	No.	Amount
NINDS:										
Funded	1258	$49,655	1215	$58,279	991	$57,159	1380	$80,212	1241	$69,555
Non-competing	886	33,349	814	37,437	742	38,151	622	36,468	721	47,579
Competing	372	16,306	401	20,842	249	19,008	758	43,744	520	21,976
Renewals	182	8,128	213	11,234	135	10,174	391	24,615	300	16,826
New	190	6,958	188	7,990	114	6,161	367	17,663	220	3,900
Supplementals	(177)	1,220	(161)	1,618	(226)	2,673	(109)	1,466	(107)	1,250
Percent funded:										
Competing	58%		63%		30%		79%		52%	
Total	82		84		63		87		72	
Unfunded	267	9,944	235	8,687	576	25,250	206	9,577	475	36,574
Renewals	107	4,325	76	3,445	202	12,132	69	4,493	175	15,624
New	160	5,619	159	5,242	374	13,118	137	5,084	300	20,950
NIAID:										
Funded	1134	50,500	1126	55,398	1023	56,521	1123	63,464	928	56,690
Non-competing	875	38,296	767	38,086	744	41,667	820	43,166	736	44,318
Competing	259	12,204	359	17,312	279	14,854	303	20,298	192	12,372
Renewals	133	7,395	184	9,973	133	7,541	146	9,899	84	5,262
New	126	4,643	175	7,211	146	7,034	157	10,045	108	6,830
Supplementals	(10)	166	(7)	128	(16)	279	(19)	354	(15)	280
Percent funded:										
Competing	50%		57%		38%		39%		24%	
Total	81		81		69		70		60	
Unfunded	261	8,436	270	8,866	457	20,141	473	23,650	614	31,937
Renewals	95	3,488	92	3,226	144	7,385	134	8,265	216	12,030
New	166	4,948	178	5,640	313	12,756	339	15,385	398	19,907
NIGMS:										
Funded	1150	75,313	1218	83,886	1290	83,210	1423	88,081	1363	81,925
Non-competing	784	53,601	719	54,553	963	59,544	918	55,420	1152	66,715
Competing	366	21,712	499	29,333	327	23,666	505	32,661	211	15,210
Renewals	165	11,029	207	13,960	154	14,259	196	17,141	98	8,884
New	201	9,549	292	14,354	173	8,884	309	14,650	113	5,780
Supplementals	(42)	1,134	(39)	1,019	(24)	523	(34)	870	(21)	546
Percent funded:										
Competing	38%		51%		29%		44%		18%	
Total	66		72		61		69		59	
Unfunded	593	21,420	485	19,178	808	33,449	634	26,325	941	39,074
Renewals	189	8,448	122	7,326	133	7,424	108	6,055	160	8,987
New	404	12,972	363	11,852	675	26,025	526	20,270	781	30,087
NICHD:										
Funded	748	42,339	907	54,663	879	55,090	1052	74,918	940	62,042
Non-competing	534	30,022	508	31,648	630	39,655	608	40,186	745	48,421
Competing	214	12,317	399	23,015	249	15,435	444	34,732	195	13,621
Renewals	73	3,873	103	7,177	75	5,713	129	11,244	55	4,621
New	141	8,074	296	15,368	174	9,300	315	23,148	140	8,660
Supplementals	(14)	370	(20)	470	(32)	422	(20)	340	(20)	340
Percent funded:										
Competing	28%		47%		31%		45%		20%	
Total	57		67		61		66		54	
Unfunded	559	20,928	445	22,447	562	27,786	551	27,411	785	46,379
Renewals	173	7,286	101	6,137	101	5,530	133	7,011	206	13,379
New	386	13,642	344	16,310	461	22,256	418	20,400	579	33,000
NEI:										
Funded	411	18,517	421	23,373	405	22,445	433	27,521	410	25,460
Non-competing	294	12,944	291	16,511	287	16,547	276	17,134	303	18,570
Competing	117	5,573	130	6,862	118	5,898	157	10,387	107	6,890
Renewals	57	3,307	53	3,395	45	2,946	68	4,896	41	2,957
New	60	2,216	77	3,278	73	2,807	89	5,410	66	3,883
Supplementals	(2)	50	(9)	189	(10)	145	(5)	81	(4)	50
Percent funded:										
Competing	69%		54%		47%		58%		39%	
Total	89		79		76		79		71	
Unfunded	52	2,736	112	4,426	131	5,582	113	7,096	166	10,866
Renewals	22	1,266	38	1,881	45	2,060	9	648	49	3,523
New	30	1,470	74	2,545	86	3,522	104	6,448	117	7,343

Regular Research Grants - Cont'd
(Amounts in thousands)

	1971		1972		1973		1974		1975	
	No.	Amount	No.	Amount	No.	Amount	No.	Amount	No.	Amount
NIEHS:										
Funded...........	112	$6,466	128	$8,966	138	$8,874	189	$12,894	151	$8,716
Non-competing..	63	4,219	76	5,667	100	6,286	91	6,270	120	7,041
Competing......	49	2,247	52	3,299	38	2,588	98	6,624	31	1,675
Renewals.....	14	593	19	1,319	13	1,327	22	1,792	9	608
New..........	35	1,632	33	1,661	25	1,195	76	4,767	22	992
Supplementals	(3)	22	(17)	319	(57)	66	(4)	65	(5)	75
Percent funded:										
Competing......	46%		45%		30%		59%		16%	
Total..........	66		67		61		73		48	
Unfunded.........	57	2,623	63	3,153	90	4,789	68	3,130	161	7,481
Renewals.......	9	533	8	694	11	678	16	955	49	2,863
New............	48	2,090	55	2,459	79	4,111	52	2,175	112	4,618
SUBTOTAL, RESEARCH:										
Funded...........	9364	487,908	9861	584,723	9534	608,249	10963	746,417	10428	706,823
Non-competing..	6622	334,434	6223	372,503	6983	432,848	6666	452,151	7504	516,997
Competing......	2742	153,474	3638	212,220	2551	175,401	4297	294,266	2924	189,826
Renewals.....	1287	71,727	1582	98,048	1097	86,162	1866	132,483	1296	87,169
New..........	1455	74,336	2056	103,253	1454	76,728	2431	150,419	1628	93,590
Supplementals	(698)	7,411	(714)	10,919	(811)	12,511	(603)	11,364	(474)	9,067
Percent funded:										
Competing......	49%		57%		37%		50%		34%	
Total..........	76		78		69		72		64	
Unfunded.........	2915	125,836	2782	117,192	4344	195,702	4261	211,936	5789	332,369
Renewals.......	1017	54,302	831	42,914	1204	60,968	1162	65,027	1711	105,873
New............	1898	71,534	1951	74,278	3140	134,734	3099	146,909	4078	226,496
NLM:										
Funded...........	19	590	25	640	27	665	28	900	32	950
Non-competing..	11	377	11	364	11	258	18	598	8	226
Competing......	8	213	14	276	16	407	10	302	24	724
Renewals.....	2	67	4	60	1	6	--	--	4	121
New..........	6	146	10	216	15	401	10	302	20	603
Percent funded:										
Competing......	66%		78%		80%		63%		62%	
Total..........	83		86		87		82		68	
Unfunded.........	4	78	4	183	4	221	6	222	15	452
Renewals.......	--	--	--	--	1	34	2	90	--	--
New............	4	78	4	183	3	187	4	132	15	452
TOTAL, NIH:										
Funded...........	9383	488,498	9886	585,363	9561	608,914	10991	747,317	10460	707,773
Non-competing..	6633	334,811	6234	372,867	6994	433,106	6684	452,749	7512	517,223
Competing......	2750	153,687	3652	212,496	2567	175,808	4307	294,568	2948	190,550
Renewals.....	1289	71,794	1586	98,108	1098	86,168	1866	132,483	1300	87,290
New..........	1461	74,482	2066	103,469	1469	77,129	2441	150,721	1648	94,193
Supplementals	(698)	7,411	(714)	10,919	(811)	12,511	(603)	11,364	(474)	9,067
Percent funded:										
Competing......	49%		57%		37%		50%		34%	
Total..........	76		78		69		72		64	
Unfunded.........	2919	125,914	2786	117,375	4348	195,923	4267	212,158	5804	332,821
Renewals.......	1017	54,302	831	42,914	1205	61,002	1164	65,117	1711	105,873
New............	1902	71,612	1955	74,461	3143	134,921	3103	147,041	4093	226,948

INDIRECT COST PAID ON GRANTS

Mr. Flood. Last year, remember, the heart and lung people told us they had a rate of indirect costs paid in connection with their research grants, and steadily going up, and reached 30.5 percent in 1972. We want you to tell us are these indirect costs getting out of hand? We want a table there showing the rate of these indirect costs paid for each one of the Institutes now, research grants, contracts, 1971, 1972, and 1973. And a statement as to how these indirect costs are negotiated.

[The information follows:]

Indirect costs are, by definition, those costs of an institution which cannot be readily identified with a single activity or project such as a grant or contract. Indirect costs are, for the most part, the costs of those activities commonly considered administrative or overhead; that is, space, utilities, executive offices, department heads and their staff, accounting, auditing, budgeting, et cetera. By Department policy, an institution which claims indirect costs as a charge to a grant or contract must submit, annually, a financial proposal giving an overall picture of that institution's total operations and the methodology it uses to identify and measure those indirect costs which it considers applicable to Federal grants and contracts. The proposal must be prepared in accordance with the costing concepts contained in the appropriate Federal cost principles; that is, circular A–21, for colleges and universities; circular A–87, for State and local units of government or, where governmentwide principles do not exist; that is, for nonprofit institutions and hospitals, in accordance with principles issued by the Department of Health, Education, and Welfare. Each proposal is evaluated by a professional negotiator. Until January 1974, the evaluation function was performed within the Office of the Assistant Secretary, Comptroller. In January, the function was decentralized to the Department's 10 regions where it is being performed within the Office of the Regional Comptroller, under the overall guidance of the Assistant Secretary, Comptroller.

The proposals are reviewed by the negotiator with audit assistance when necessary. The scope of the review depends upon the amount of Federal funds involved, and the confidence which the negotiator has in the reasonableness of the proposal based on his experience with the submitting institution and with other comparable institutions.

Professional judgment is an important element in the negotiation process and negotiators are expected to exercise that judgment within the parameters of policies and procedures issued by the Office of the Assistant Secretary, Comptroller. Those parameters are contained in a negotiator's staff handbook which includes among other things guidance on the scope and depth of evaluation and the use of audit systems, and a negotiation program.

Indirect costs paid under the National Institutes of Health grants and contracts are increasing. The increases, however, are explainable:

(*a*) Costs in general are going up as a result of inflationary pressures.

(*b*) Direct costs of grants are increasing and the base costs upon which overhead rates are applied, are increasing.

(*c*) Institutions in general are claiming costs which they have always been entitled to under Federal costing concepts but had not in the past.

This is not to say that all costs claimed by institutions are reasonable and acceptable or that institutions are performing at peak operational efficiency. There are cost areas which require especially hard negotiating. We are aware of those areas and are dealing with them. There has been and will continue to be a need on the part of the Federal Government to review cost proposals to assure itself that the cost assigned to Federal grants and contracts are made in accordance with generally accepted accounting concepts, and reasonably reflect benefits received by those grants and contracts. But indirect costs have not gotten out of control.

RATIO OF INDIRECT COST TO RESEARCH PROJECT GRANT DOLLARS AWARDED

Fiscal year	Total dollars awarded	Indirect cost (I/C) awarded	Percent of I/C to total award	Percent increase (decrease)
NATIONAL INSTITUTES OF HEALTH				
5-yr change, 19.12 to 24.83 percent equals 5.71 percent:				
1968	502,055,900	96,008,000	19.12	
1969	502,965,100	105,066,600	20.88	1.76
1970	482,764,700	107,198,300	22.20	1.32
1971	557,745,800	126,005,700	22.59	.39
1972	675,272,900	159,649,600	23.64	1.05
1973	720,771,600	179,038,000	24.83	1.19
NATIONAL CANCER INSTITUTE (NCI)				
5-year change, 17.99 to 22.77 percent equals 4.78 percent:				
1968	71,612,000	12,881,800	17.99	
1969	73,276,500	14,252,200	19.45	1.46
1970	71,688,300	14,735,800	20.56	1.11
1971	88,719,800	18,365,500	20.70	.14
1972	121,360,900	25,826,400	21.28	.58
1973	157,684,700	35,901,500	22.77	1.49
NATIONAL HEART AND LUNG INSTITUTE (NHLI)				
5-year change, 18.87 to 24.01 percent equals 5.14 percent:				
1968	94,814,900	17,894,000	18.87	
1969	90,571,800	18,638,700	20.58	1.71
1970	87,271,600	19,094,900	21.88	1.30
1971	109,888,800	23,689,100	21.56	(.32)
1972	126,971,300	29,565,400	23.29	1.73
1973	137,283,500	32,960,600	24.01	.72
NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES (NIAID)				
5-year change, 19.62 to 25.24 percent equals 5.62 percent:				
1968	48,879,900	9,592,500	19.62	
1969	51,961,100	10,945,200	21.06	1.44
1970	48,687,800	10,942,600	22.48	1.42
1971	51,579,700	12,203,700	23.66	1.18
1972	57,796,600	14,151,200	24.48	.82
1973	58,908,900	14,868,500	25.24	.76
NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT (NICHD)				
5-yr change, 20.41 to 26.28 percent equals 5.87 percent:				
1968	38,060,200	7,767,100	20.41	
1969	37,776,600	8,361,500	22.13	1.72
1970	39,941,700	8,880,600	22.23	.10
1971	46,970,400	10,461,900	22.27	.04
1972	60,343,400	14,433,600	23.91	1.64
1973	60,697,700	15,951,600	26.28	2.37
NATIONAL INSTITUTE OF GENERAL MEDICAL SCIENCES (NIGMS)				
5-yr change, 18.97 to 25.29 percent equals 6.32 percent:				
1968	75,232,400	14,273,900	18.97	
1969	75,061,000	15,106,900	20.13	1.16
1970	69,927,500	15,158,400	21.68	1.55
1971	79,306,200	18,072,700	22.79	1.11
1972	94,866,800	22,497,800	23.72	.93
1973	95,726,900	24,206,300	25.29	1.57
NATIONAL INSTITUTE OF NEUROLOGICAL DISEASES AND STROKE (NINDS)				
5-yr change, 19.50 to 25.76 percent equals 6.26 percent:				
1968	65,143,100	12,706,000	19.50	
1969	52,855,800	11,637,000	22.02	2.52
1970	49,034,600	11,403,000	23.26	1.24
1971	53,790,100	12,689,400	23.59	.33
1972	64,109,900	15,995,600	24.95	1.36
1973	62,849,200	16,191,200	25.76	.81

RATIO OF INDIRECT COST TO RESEARCH PROJECT GRANT DOLLARS AWARDED—Continued

Fiscal year	Total dollars awarded	Indirect cost (I/C) awarded	Percent of I/C to total award	Percent increase (decrease)
NATIONAL INSTITUTE OF DENTAL RESEARCH (NIDR)				
5-yr. change, 23.04 to 27.47 percent equals 4.43 percent:				
1968	14, 469, 800	3, 333, 400	23. 04	-------------
1969	15, 142, 800	3, 448, 400	22. 77	(.27)
1970	14, 658, 900	3, 594, 100	24. 52	1. 75
1971	16, 856, 700	4, 111, 100	24. 39	(.13)
1972	20, 696, 900	5, 158, 900	24. 93	. 54
1972	21, 227, 000	5, 831, 600	27. 47	2. 54
NATIONAL EYE INSTITUTE (NEI)				
5-yr. change, 20.73 to 27.04 percent equals 6.31 percent:				
1968	524, 900	108, 800	20. 73	-------------
1969	14, 960, 700	3, 339, 600	22. 32	1. 59
1970	16, 199, 700	3, 842, 700	23. 72	1. 40
1971	19, 203, 000	4, 597, 400	23. 94	. 22
1972	23, 284, 500	5, 990, 900	25. 73	1. 79
1973	22, 444, 600	6, 069, 800	27. 04	1. 31
NATIONAL INSTITUTE OF ARTHRITIS, METABOLISM AND DIGESTIVE DISEASES (NIAMDD)				
5-yr change, 18.51 to 25.96 percent equals 7.45 percent:				
1968	85, 369, 500	15, 805, 600	18. 51	-------------
1969	83, 221, 100	17, 427, 800	20. 94	2. 43
1970	77, 979, 600	17, 754, 900	22. 77	1. 83
1971	81, 915, 100	19, 511, 500	23. 82	1. 05
1972	93, 487, 500	23, 011, 900	24. 61	. 79
1973	91, 332, 200	23, 708, 800	25. 96	1. 35
NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES (NIEHS)				
5-yr change, 20.69 to 26.54 percent equals 5.85 percent:				
1968	7, 949, 200	1, 644, 900	20. 69	-------------
1969	8, 137, 700	1, 909, 300	23. 46	2. 77
1970	7, 375, 000	1, 791, 300	24. 29	. 83
1971	9, 516, 000	2, 303, 395	24. 21	(.08)
1972	12, 355, 100	3, 017, 900	24. 43	. 22
1973	12, 616, 900	3, 348, 100	26. 54	2. 11

Mr. Flood. Mr. Shriver.

TRAINING GRANTS

Mr. Shriver. Thank you, Mr. Chairman.

You are proposing a phaseout of research training grants, and they are to be replaced in some measure by individual fellowships on a competitive basis. Is that correct?

Dr. Stone. Yes, sir, that is generally true.

Mr. Shriver. I presume you feel you have adequate information on which to base this change?

Dr. Stone. We are using informed best judgment rather than specific data. There are no precise numbers that tell us how many immunogeneticists the country ought to have next year. But we are trying to judge on the basis of research activity and individuals who are in the field what seems to be a reasonable number.

SURVEY BY THE NATIONAL ACADEMY OF SCIENCES

Mr. Shriver. I brought it up because I understood the National Institutes of Health requested a statistical survey from the National Academy of Sciences which would show results of past training in the fellowship programs—things like identifying the differences in career patterns between National Institutes of Health beneficiaries and students who did not receive National Institutes of Health support. Has that been completed?

Dr. STONE. Perhaps we can give you a status report.

Dr. KENNEDY. It hasn't yet been completed.

Mr. SHRIVER. When is it expected?

Dr. KENNEDY. I think it is due about a year from now.

SURVEY OF THE ASSOCIATION OF AMERICAN MEDICAL COLLEGES

Mr. SHRIVER. One survey by the Association of American Medical Colleges shows that over half of the biomedical research students and medical students indicated they could not have completed their training if low interest loans had been substituted for training grants, fellowships, or stipends. Do your studies indicate the same thing? Have you made any comparable studies?

Dr. KENNEDY. No; we have nothing yet in, but we are watching fairly carefully first year graduate enrollments to indicate how many people are matriculating as doctor of philosophy candidates—and annual doctor of philosophy awards, both in general, and in the specific fields in which we are interested.

The difficulty here, Mr. Shriver, is that the data tend to become available after a considerable lag. The annual survey performed by the Office of Education is the key element here and somehow there is a considerable lag time in getting the results published. But we are going to watch very carefully and will propose corrective action if graduate enrollment or doctor of philosophy output falls sharply.

Mr. MILLER. I am not sure whether part of that, if statistics prove valid, is because the law currently puts a limit of $10,000 on the amount of loan. But we have legislation before the Congress to increase that amount to $25,000.

Mr. SHRIVER. Even that won't be enough, will it, for this kind of training?

Mr. MILLER. I would have to defer to the National Institutes of Health. It certainly is a significant increase.

COST OF TRAINING A SCIENTIST

Mr. SHRIVER. What would be your suggestion? What does it cost to train a scientist or doctor of philosophy?

Dr. KENNEDY. We are talking in the neighborhood of $30,000 to $40,000. Most people take 5 to 6 years to get their doctor of philosophy and most scientists thereafter require at least a year or two of postdoctoral training. By that time they are fairly well along and are beginning to pickup responsibilities and their living expenses are getting pretty high.

Mr. SHRIVER. And if they are paying for it themselves through loans they are in pretty heavy debt.

Dr. KENNEDY. Physicians who go into research traditionally complete their residency training first and only thereafter go into a research training experience, which they enter into at approximately age 30. Two or three more years is a pretty expensive proposition for them at that stage in their careers.

PUBLIC LAW 480 PROGRAM

Mr. **Shriver**. There was one comment on page 9 of your statement where you referred to the excellent example of the importance of international cooperation in research in the value of the Public Law 480 program. I certainly agree with that. You say "foreign currencies will, unfortunately, soon be exhausted." Are you referring just to Israel?

Dr. **Stone**. No.

Mr. **Shriver**. We have billions of dollars in foreign currencies in other countries.

Mr. **Miller**. It certainly doesn't apply to Israel because that has been exhausted for quite a few years.

Dr. **Stone**. Yugoslavia has been exhausted. There is money left in Poland. India has a substantial amount of money.

Mr. **Flood**. Is there any left in Poland?

Dr. **Stone**. We are still proposing programs for Poland. In India, where there is an enormous amount of money, there are problems of how the money is to be spent. The Indian Government has considerable say in that and they are less interested in biomedical programs than in other programs.

Mr. **Shriver**. I think our Ambassador over there got some of these excess currency funds turned back.

I think it might be well at this point to put in the record, if you don't have that with you, foreign currencies that have not been exhausted. I ask this question because I also serve on the Foreign Operations Subcommittee on Appropriations which deals with appropriations for foreign countries.

[Clerk's Note: The information requested was not supplied by the Department.]

GENERAL RESEARCH SUPPORT GRANTS

You are proposing to terminate General Research Support Grants. You say this aid was going to a few favored institutions.

Dr. **Stone**. No, sir. I don't mean in the sense of favoritism. Essentially, it went in largest amounts to the most successful institutions. Because the amount of the GRS awards was partly determined by how much research funds an institution had received, the most successful institutions got the most additional money. That is what we mean by "favored."

Mr. **Shriver**. We have been getting quite a bit of mail, as you can imagine, on this proposed cutback. One letter I received from an independent research institution raised the point that their particular type of institution would especially suffer from an end to general research support. They say they are more dependent on this type of aid than the university-affiliated institutions. Would you care to comment on that?

Dr. **Stone**. I don't know why that should be the case unless it has something to do with the endowment available to that particular research institute.

Mr. **Schwartz**. Perhaps it is due to the fact that they are not State-supported, and therefore, if there are any gaps in Federal spending, it could not be picked up by the State.

Mr. **Shriver**. They are independent research institutions.

Mr. **Schwartz**. Yes.

MULTIPLE SCLEROSIS

Mr. SHRIVER. Has NIH received the report from the National Advisory Commission on Multiple Sclerosis?

Dr. STONE. We have that and I might suggest, sir, that you pursue that when Dr. Towers testifies for NINDS.

Mr. SHRIVER. Would you put into the record how much is in this budget for research in this field?

Dr. STONE. Yes, sir.

Mr. SHRIVER. And how much is in this request for diabetes research and how that compares with former years.

[The information follows:]

Amount in fiscal year 1975 budget request for research in:

[In thousands of dollars]

	1973	1974	1975 estimate
Multiple sclerosis	4,212	4,493	4,295
Diabetes	8,235	12,414	11,921

HEALTH RESEARCH EQUIPMENT

Mr. SHRIVER. The General Accounting Office issued a report last year entitled "Better Management Needed of Health Research Equipment by NIH Grantees." The report was pretty critical on the lack of control that you seemed to have in regard to the use of equipment purchased with grant funds. Would you care to comment on that report, and what has been done in response to the criticism?

Dr. STONE. I will ask Mr. Schwartz to do that because he has looked specifically into that problem, not only for NIH but for another agency.

Mr. SCHWARTZ. We have sent a copy of that report to every one of our grantees. We felt it was quite serious and that the institutions were not doing their research dollar full justice by not fully utilizing the equipment that was available to them. This was the first part of our approach—just to make the institutions aware of this deficiency.

The second part of our approach will be to develop a set of guidelines as to what constitutes a good equipment management system. We will then work with a number of institutions to put it into place and develop some examples of good equipment utilization.

We hope in that way to get one university to assist and support another university. We hope, by the end of fiscal year 1975, to have a complete set of guidelines available for all universities as to what their equipment utilization systems should look like.

Mr. SHRIVER. Thank you.

Mr. FLOOD. Mr. Natcher.

TRAINING GRANTS AND FELLOWSHIPS

Mr. NATCHER. Dr. Stone, I want to return just a moment to one of my chairman's questions and especially that portion he read to you out of the report concerning training grants and fellowship programs.

On page 10 of your statement you point out the change that is to take place by virtue of the new program announced by the Secretary. I am wondering, Dr. Stone, if this is going to give us adequate training. You know before we mark this bill up we will probably hear quite a bit from deans of colleges of medicine and a great many other people that are very much concerned about this particular matter.

Would you say to the committee now, Dr. Stone, there will be adequate training under this proposed change that you have here?

Dr. STONE. I would like to share this.

Mr. NATCHER. Go right ahead.

Dr. STONE. Would you care to comment on the adequacy of training we might have, Dr. Stetten.

Mr. NATCHER. Will it be adequate? We are very much concerned about this matter on this committee and I know my chairman will hear quite a bit about it before we mark this bill up. Is there adequate training provided for here? When you say "Opportunities for training individuals in particular health sciences or related fields in which there is a manpower shortage there will be a limited number of institutional research fellowship awards." Will this provide us with the adequate training that we consider necessary and that you believe in at this time?

Dr. STETTEN. It is a very difficult subjective judgment, Mr. Natcher, and I cannot claim to be in total agreement will all parts of the Administration's proposal.

I would like to see everybody with high intelligence devoting their entire lives to biomedical research, but this is patently preposterous. There are other careers to be followed.

I think the proposal, as written, can be watched and tested against the number of applicants with high qualification who seek admission into this field. If we can supply training funds for a substantial fraction of what the institutions consider to be well-qualified applicants, then that meets the test of adequacy. I think that for the time being we may well be able to approach this goal, but we will have to wait a year or two to see. I can't give a very specific answer to this question. I am not sure it has a specific answer.

Mr. NATCHER. I can understand your position. Dr. Stone, this is a right important matter. You know you have a lot of good people around you, Doctor. I am hoping you watch this matter because I have my doubts about it. You gentlemen know and I don't know, but I have my doubts about the system you are proposing at this time.

Mr. Chairman, I just thought I had better say that.

Dr. STONE. The system does have built-in alarms, and I am sure that those early warning alarms will work and that we will get the message if we are falling short.

Mr. NATCHER. Thank you, Mr. Chairman.

Mr. FLOOD. Mr. Patten.

TRAINING GRANTS

Mr. PATTEN. Thank you, Mr. Chairman.

This is April. Thirty fellows working at the Rutgers Biomedical Institute will be coming back and they ought to know now and not when you get that early warning alarm. I understand this is one place under the new policy where 30 people, highly respected, will be discharged and unable to stay in school. They were upset enough about this; they had me give up part of my Christmas weekend to go up there and listen to them for 4 or 5 hours.

At least as far as those people are concerned the time of decision I think is now. I don't think they can put that off.

Dr. STONE. Might I call upon Dr. Thomas Malone, who is in charge of that particular area of support for NIH, to give us a status report and tell us where we are in the selection of those fellows for next year.

Dr. MALONE. I think you are probably referring to predoctoral students. The new program lends itself only to postdoctorals.

The applications for that program were in as of February 1. They are being reviewed in March and April and the awards will be made in May and June.

Unfortunately, if a candidate had not already been allied with a training program under the old system and if we had not already made a commitment to that individual, that individual will fall through the gap in the transition between the old and the new.

Mr. PATTEN. In other words, the work of the fellows working for doctorate, their work is aborted? That is what you are saying. The answer is I might as well tell them to go home right now? The new policy is postdoctoral. These fellows are working for doctor's degrees. They have their M.A. So there is no use waiting. I might as well call them this afternoon and say "fellows, you are finished, you are not going to be back in school next year." That is if I understood you.

Mr. MILLER. I need to ask a question, Mr. Chairman, so I can learn. I may get the wrong answer, but it is my understanding that we are not allowing any of our commitments to lapse. If a student already has a fellowship or a training grant, he can complete his course of study. It is new commitments we are not beginning.

Dr. MALONE. That was the statement I made.

Mr. PATTEN. You think the fellows onboard now then are set to continue? They didn't have that impression at Christmas time.

Dr. MALONE. If they are already allied with previous training activities, under the old training program, they can continue to the completion of their degrees. If they had no relationship to that program, then they would not qualify for the new postdoctoral fellowship program.

CANCER

Mr. PATTEN. Let's go back to Dr. Stone. With the same philosophy you are going to add another $100 million for cancer, as in the December 2 campaign speech. I am not referring to the President. It led us to believe we are going to have a space program to cure cancer. I remember one prominent person who already said it gave that impression. So those were the headlines.

Now we go up to $600 million. Some of the people in our universities feel they are not in on this either under your new program. They have a lot of ideas and feel they have done a lot of work and feel they are not getting a square deal.

It is hard for us to sit here and pass judgment. I know the applications for cancer money apparently have not been accepted. They weren't honored.

RELEASED 1973 FUNDS

Tell me, Mr. Miller, with all of these court orders to pay all the 1973 impounded money and disburse all the other money, do you have all the money you need?

Mr. **Miller.** I think the Secretary made a very explicit statement on that, Mr. Patten, that no funds are impounded and the money will all be obligated.

Mr. **Patten.** Have you got it?

Mr. **Miller.** We've got it.

Mr. **Patten.** You don't need another supplemental? Like paying a judgment, a fellow gets sued and has a judgment and has to go out and find the money.

Mr. **Miller.** I think the language that has been included in the two most recent supplementals, plus the language in the court orders have clearly made the money available. It hasn't lapsed to the Treasury. The money is available for obligation. In fact, we have rulings from both the General Accounting Office and the Treasury Department to that effect.

Mr. **Patten.** Mr. Natcher expressed his concern, and I listened with great attention to the statement of the chairman, and I don't want to go over that ground again. So at this time I have no further questions, Mr. Chairman.

Mr. **Flood.** Mr. Obey.

Mr. **Obey.** Thank you, Mr. Chairman.

ADEQUACY OF NIH BUDGET

I think most of the questions I wanted to ask have already been asked. Let me pursue a few.

Dr. Stone, whenever anybody on this side of the table asks somebody in your seat about the adequacy of the budget, they always cite the fact that you have other budget constraints and so they are really not in a position to talk very much about it. Recognizing that, I would like to ask you just about the same question the chairman did but see if I couldn't pursue it a little further.

Recognizing that we do have budget constraints, recognizing also that Cancer and Heart have been the only Institutes really which have grown in real terms because of inflation effect—and you can question whether Heart and Lung has—giving your best professional judgment, could you elaborate a little more on the answer you gave to the chairman on the adequacy of the budget for NIH in Institutes other than Cancer and Heart and Lung?

Dr. **Stone.** Yes. Within the money that is available, Institute Directors have made difficult decisions about the areas they can support. In each Institute, I know from conferences with Institute Directors and from their advisory councils, that there are good scientific opportunities that they would like to see exploited.

One doesn't cut out whole blocks of programs. Let's say that for diabetes research, to again use that example, we provide some x million dollars of support. Nevertheless, there will unquestionably be some good proposals having to do with research on diabetes that we cannot support because we must also support research in other areas.

So we could say that if more money were available—if the administration and the Congress together were to make more money available—we believe it could be well spent in exploiting good scientific opportunities.

Mr. Obey. Last year—I forget who said it but it was implied several times—when we went over all of the Institutes' budgets, whenever the question was raised about the percentage of grant applications which had been turned down, it was implied, at least in some quarters, that, well, that may have been simply because we have too many researchers around the country.

What you are saying, in effect, is that you can in other Institutes besides Cancer and Heart and Lung utilize with a high degree of probable effectiveness substantially larger funds than have been proposed. I think I am not putting words in your mouth.

Dr. Stone. I think that is accurate with the exception of a problem over what "substantial" means. I am not used to the Federal Government yet, and some figures that you might regard as small I regard as substantial. Certainly there are research applications that have been approved, that have gone through rigorous peer review, that we are not able to fund. That certainly does exist; yes, sir.

EMPLOYMENT CEILINGS

Mr. Obey. Attention has been drawn recently to the subject of position ceilings. The chairman again mentioned it today. You or someone else indicated that position ceilings were not forcing you to cut back this year.

Let me ask this: At the time of his resignation Dr. Sherman mentioned particularly the feeling that one demonstrable indication of support by the administration for NIH would be the addition of additional positions. I noted that in Dr. Edwards' speech made on NIH on February 21 he said:

> Moreover I would like to emphasize that their—

Meaning Dr. Stone's and Dr. Stetten's—

> recommendations will be given, as indeed they have already been given, every possible consideration in the decisionmaking process not just with respect to biomedical research as it concerns the National Institutes of Health but with respect to the entire health efforts for which my offices are responsible.
>
> Let me give you one illustration of this particular point. I have had lengthy discussions with Dr. Stone and Dr. Stetten in which they have forcibly and very articulately presented the critical personnel problems they face on the campus, and I am convinced that the National Institutes of Health intramural research has been jeopardized and will continue to suffer if these acute manpower problems are not met.
>
> Dr. Stone and I have carried this message personally to Secretary Weinberger, and I think that we are going to be able to find some relief to this problem in the very near future. So obviously we will rely on Dr. Stone and his colleagues to determine how additional personnel can most successfully be utilized to help fill NIH's most pressing manpower needs.

My question is what tangible—you were talking about what you have done intangibly—what tangible consequences of Dr. Edward's apparent agreement on this subject with Dr. Stone are there that we can put our finger on on this side of the table?

Dr. Stone. I asked Dr. Edwards this morning, as I anticipated this would come up, whether he had any information for me and Dr.

Edwards told me he continues to be optimistic that we would have help. I was therefore interested in Mr. Miller's comment earlier in this hearing and I wonder if he can clarify what he said.

Mr. Miller. I think we can be quite specific, Mr. Obey, and I thought I had given that answer when I was discussing the same question with the chairman.

I think we have made it quite clear—and it has resulted from the very kind of discussion you quoted in the record—that we are going to provide NIH with more ceiling. I believe it is in the nature of 200 more employment ceiling in fiscal year 1974.

Mr. Obey. The chairman asked you to place it in the record but I am wondering if you could give me some information now.

From fiscal 1968 through fiscal 1974 how many positions were cut at NIH?

Mr. Schwartz. In 1968 our ceiling was 10,991. Our current ceiling for fiscal year 1974 is 10,395. Of course if we get the relief this number would go up by the 200.

Mr. Obey. Then that is 200 positions, but you have added at cancer during that time what, 300 or thereabouts?

Mr. Schwartz. Yes, sir, the Cancer Institute has gone up by 367 from 1968 to 1974.

Mr. Obey. So you have actually had a net reduction in other Institutes of around 700 then?

Mr. Schwartz. Yes.

Mr. Obey. Since 1968?

Mr. Schwartz. Yes.

Mr. Obey. 200 isn't going to do much to change that is it?

Mr. Schwartz. We have looked very carefully at our needs, and we feel that with the additional 200 positions we would be able to fully staff the clinical center at a level which would allow it to operate at maximum capacity, maximum capacity being around 75 percent. We feel that, along with the addition of 54 positions in the next fiscal year, we will be able to open up the new perinatal facility currently under construction at the clinical center, and we feel that we would have adequate support in the heart and lung institute to be able to carry out their new legislative mandates. These are the two areas that will be the prime recipients of additional positions.

Mr. Obey. Will all of the Institutes receive some additional positions?

Mr. Schwartz. Virtually all of the Institutes will receive some positions, yes, sir.

Mr. Obey. Ranging from what to what?

Mr. Schwartz. This is based upon some studies we have done of our internal operation. For Child Health Institute will be receiving, over the 2 years, something like 15 positions and that is the highest.

Mr. Obey. How about the Environmental Institute?

Mr. Schwartz. The Environmental Institute, over the 2 years, will be going up about 10.

Mr. Obey. Ten?

Mr. Schwartz. Yes, sir. This is from fiscal 1973.

Mr. Obey. What do they have now?

Mr. Schwartz. The Environmental Institute currently has 233 positions.

Mr. OBEY. That is a pretty small percentage.

Mr. SCHWARTZ. When the Environmental Institute building program is completed, and they do have their planning under way, this number will have to increase considerably. At the moment they are somewhat constrained by facilities.

Mr. OBEY. How about General Medical?

Mr. SCHWARTZ. General Medical Science Institute is at 155 but they have no intramural programs. So you will find their number will be much less than the other Institutes.

Mr. OBEY. So you will be restoring about 200 of the some 700 positions that have been cut since 1968.

Let me ask you this, Doctor. To give credit where credit is due, I am looking at some views of Representative Dingell which he wrote as a supplement to the report on the National Diabetes Act of 1974. He has some interesting statistics in here.

He says "Special initiative programs have doubled over the 1968–73 period while all other biomedical research programs have increased by about 5 percent."

I know that Congress in some instances has been as guilty of selecting "the disease of the month" as the administration has, but I know virtually nothing about medicine, or science for that matter, in comparison to a health professional.

I would think that would be an awfully dangerous trend we are following right now. Do you think 200 positions will be adequate to reverse it?

Dr. STONE. No, I don't think it will have a substantial impact on this. It isn't a quantitative matter. I think you are discussing an issue that is qualitatively different.

Certainly, there are constituencies and pressure groups and concerned individuals who back the disease-of-the-month approach. Certainly, one has misgivings about that and has mixed feelings about it.

On the one hand, it does provide initiative and impetus to develop an area. On the other hand, perceptions of nonscientists about where the money can best be spent are often emotional or ill-informed, and they don't represent, in many ways, the scientist's most objective view of where it is possible to make research findings.

An example that has gotten a great deal of publicity is the Sudden Infant Death Syndrome. I think all scientists would share the deep emotional concern of parents who have lost babies due to this particular disease. There is no question about that. On the other hand, it is a baffling disease, and it is not at all clear that putting an enormous sum of money into research on that disease would be a productive way to spend the money. That is an example, rather more clear-cut than some, where we believe that fundamental research—on mechanisms of breathing, of respiration, of the heart beat, in the brain and central nervous system—must go on before we are able to even approach the matter of saving those babies.

On that account scientists want to be more circumspect in drives on a particular disease and that is the reason for their intense concern about the development of the underlying knowledge that undergirds all attacks on disease. When one makes fundamental findings about how cells work, the relationship between cells, how the genes of a cell control what the body will be like, that is the knowledge that is most likely to be valuable, often in most unexpected ways, in the attack on one or another disease.

We certainly have substantial reservations about the disease of the month approach.

I have read Mr. Dingell's comments. I think they are extremely perceptive and very useful in bringing a viewpoint into prominence that has to be considered.

SUPPORT FOR CANCER AND HEART AND LUNG

Mr. OBEY. I notice, and this is the only comment I have on this:

> The percentage distribution of NIH research support for Cancer and Heart and Lung in 1968 is 31 percent; all other Institutes 69 percent. By 1974 it had reached 50 percent for Cancer, Heart and Lung and all other Institutes 50 percent. In dollar amounts, while Cancer and Heart had a great deal more than doubled in that time from $320 to $765 million, all other Institutes had only increased by $66 million.

Dr. STONE. Yes.

ADVISORY COMMITTEE

Mr. OBEY. Let me ask on another subject. There have been references in the newspapers to the so-called "politicalization" of the advisory apparatus on which NIH is dependent for the quality of its selection of research projects. Will you provide for the record data over the period of 1965 to 1973 of the numbers of times when the nominations from within NIH for professional members of the Institutional Advisory Councils have been set aside in favor of other individuals suggested by higher echelons?

Dr. STONE. We will do so. I understood your question to be specifically related to professional scientific membership on the Council.

Mr. OBEY. Professional members.

Dr. STONE. Yes, sir.

[The information follows:]

ANALYSIS OF APPOINTMENTS OF PROFESSIONAL MEMBERS OF NIH ADVISORY COUNCILS (1965–1973)

The following list includes all advisory groups for which NIH nominates candidates but for which appointments are made by the Secretary. The usual procedure is for NIH to nominate one candidate and one alternate for each vacancy. If neither of the names suggested is acceptable, the Office of the Secretary may request additional nominations and this process is sometimes repeated. An invitation to serve on an advisory group is sent by the Secretary either to one of those nominated by NIH or to another candidate. Although nominations are routinely submitted four months before a scheduled vacancy occurs, the selection process frequently takes as much as a year—longer, in exceptional cases. The tables show the vacancies remaining at the end of each calendar year.

In addition to the legislatively established National Advisory Councils for the NIH Institutes and the Division of Research Resources, the following table includes:

The Director's Advisory Committee which was appointed in 1967, on the recommendation of the Wooldridge committee, to advise the Director, NIH;

The Sickle Cell Disease Advisory Committee which was established, pursuant to a Presidential initiative, in 1971;

The Hypertension Information and Education Advisory Committee which was established by former Secretary Richardson in 1972;

The Board of Advisers for the Fogarty International Center which was appointed in 1972. However, the decision to create such a body was reconsidered and withdrawn by NIH in March 1973, before the Board had actually met.

The Board of Regents of the National Library of Medicine for which NIH suggests candidates but for which nominees are submitted by the President for confirmation by the Senate.

The National Advisory Cancer Council was superseded in 1972 by the National Cancer Advisory Board established by the National Cancer Act of 1971. In anticipation of this legislation, new appointments to the National Advisory Cancer Council were suspended during 1971. Appointments to the Board are made by the President on the basis of nominations received from a number of sources and are therefore not included in the following tabulation.

An Environmental Health Program Advisory Committee was established, by the Director, NIH, on November 30, 1966. It was reestablished, on March 18, 1967, as the Environmental Health Sciences Advisory Committee by the Surgeon General, with approval of the Secretary, and was renamed the National Advisory Environmental Health Sciences Council on December 16, 1971. Since 1968 nominations for vacancies have been submitted to the Secretary for final approval and are thus included in the table.

Membership in the National Advisory Councils, established by law for each of the Institutes, usually consists of eight professional members, with expertise in the scientific or clinical areas of concern to the Council, and four lay members, with an interest in the work of the Institute that the Council serves. The following tables refer only to the professional members of the Councils and of the other advisory groups; the appointment of lay members has been excluded from the data because their selection is based on their general interest and civic leadership rather than their professional scientific competence.

Analysis of Appointments of Professional Members of NIH Advisory Councils

(1965 - 1973)

SUMMARY PAGE

	1965	1966	1967	1968	1969	1970	1971	1972	1973
Vacancies	19	21	30	26	38	42	39	62	49
NIH Candidates	41	49	49	56	78	85	54	112	76
NIH Candidates Approved	21	23	32	27	38	36	25	37	19
Other Candidates	2	1	0	0	1	10	9	11	6
Invited	23	24	32	27	39	46	34	45	25
Declined	5	3	2	1	3	6	1	3	1
NIH Candidates Appointed	16	20	30	26	36	32	24	34	19
Other Candidates Appointed	2	1	0	0	0	8	9	8	5
Remaining Vacancies	1	0	0	0	2	2	6	20	25

Analysis of Appointments of Professional Members of NIH Advisory Councils

(1965 - 1973)

	1965	1966	1967	1968	1969	1970	1971	1972	1973
Director's Advisory Committee									
Vacancies	ne	ne	12	0	2	12	2	5	2
NIH Candidates	—	—	12	0	2	27	4	9	6
NIH Candidates Approved	—	—	12	0	2	10	2	4	0
Other Candidates	—	—	0	0	0	4	0	0	0
Invited	—	—	12	0	2	14	2	4	0
Declined	—	—	0	0	0	2	0	0	0
NIH Candidates Appointed	—	—	12	0	2	8	2	4	0
Other Candidates Appointed	—	—	0	0	0	4	0	0	0
Remaining Vacancies	—	—	0	0	0	0	0	1	2

ne = not in existence

	1965	1966	1967	1968	1969	1970	1971	1972	1973
Cancer Council									
Vacancies	3	3	2	2	2	2	#	na	na
NIH Candidates	7	6	4	4	4	5	—	—	—
NIH Candidates Approved	1	2	2	2	2	1	—	—	—
Other Candidates	1	1	0	0	0	1	—	—	—
Invited	2	3	2	2	2	2	—	—	—
Declined	0	0	0	0	0	0	—	—	—
NIH Candidates Appointed	1	2	2	2	2	1	—	—	—
Other Candidates Appointed	1	1*	0	0	0	1	—	—	—
Remaining Vacancies	1	0	0	0	0	0	—	—	—

* White House appointment
# White House instructed NCI to hold up all nominations pending implementation of National Cancer Act.
na = not applicable

	1965	1966	1967	1968	1969	1970	1971	1972	1973
Heart and Lung Council									
Vacancies	2	2	2	2	2	4	3	4	2
NIH Candidates	4	4	4	4	4	7	4	9	4
NIH Candidates Approved	2	2	3	2	2	4	2	4	1
Other Candidates	0	0	0	0	0	0	1	0	1
Invited	2	2	3	2	2	4	3	4	2
Declined	0	0	1	0	0	0	0	0	0
NIH Candidates Appointed	2	2	2	2	2	4	2	4	1
Other Candidates Appointed	0	0	0	0	0	0	1	0	1
Remaining Vacancies	0	0	0	0	0	0	0	0	0
Sickle Cell Committee									
Vacancies	ne	ne	ne	ne	ne	ne	7	1	7
NIH Candidates	—	—	—	—	—	—	10	1	10
NIH Candidates Approved	—	—	—	—	—	—	6	1	3
Other Candidates	—	—	—	—	—	—	1	0	0
Invited	—	—	—	—	—	—	7	1	3
Declined	—	—	—	—	—	—	0	0	0
NIH Candidates Appointed	—	—	—	—	—	—	6	1	3
Other Candidates Appointed	—	—	—	—	—	—	1	0	0
Remaining Vacancies	—	—	—	—	—	—	0	0	4
Hypertension Committee									
Vacancies	ne	ne	ne	ne	ne	ne	ne	12	3
NIH Candidates	—	—	—	—	—	—	—	22	6
NIH Candidates Approved	—	—	—	—	—	—	—	9	2
Other Candidates	—	—	—	—	—	—	—	3	1
Invited	—	—	—	—	—	—	—	12	3
Declined	—	—	—	—	—	—	—	1	0
NIH Candidates Appointed	—	—	—	—	—	—	—	8	2
Other Candidates Appointed	—	—	—	—	—	—	—	3	1
Remaining Vacancies	—	—	—	—	—	—	—	1	0

ne = not in existence

	1965	1966	1967	1968	1969	1970	1971	1972	1973
Dental Research Council									
Vacancies	2	2	2	2	2	2	3	2	3
NIH Candidates	4	4	4	4	5	4	6	4	4
NIH Candidates Approved	2	2	2	2	3	1	4	1	0
Other Candidates	0	0	0	0	0	1	0	0	1
Invited	2	2	2	2	3	2	4	1	1
Declined	0	0	0	0	1	1	1	0	0
NIH Candidates Appointed	2	2	2	2	2	1	3	1	0
Other Candidates Appointed	0	0	0	0	0	0	0	0	1
Remaining Vacancies	0	0	0	0	0	1	0	1	2

* Pending since May, 1973

	1965	1966	1967	1968	1969	1970	1971	1972	1973
Arthritis Council									
Vacancies	2	2	2	2	2	4	5	9	5*
NIH Candidates	4	4	4	6	3	6	5	14	6
NIH Candidates Approved	2	2	2	3	1	4	0	7	2
Other Candidates	0	0	0	0	0	0	0	0	0
Invited	2	2	2	3	1	4	0	7	2
Declined	0	0	0	1	1	0	0	0	0
NIH Candidates Appointed	2	2	2	2	0	4	0	7	2
Other Candidates Appointed	0	0	0	0	0	0	0	0	0
Remaining Vacancies	0	0	0	0	2	0	5	2	3

* In March 1974, of 2 OS candidates and 1 NIH candidate invited, there was 1 OS acceptance, 1 OS declination and 1 NIH acceptance.

	1965	1966	1967	1968	1969	1970	1971	1972	1973
Neurology Council									
Vacancies	2	3	1	2	4	3	1	2	2
NIH Candidates	4	6	2	4	8	7	3	5	4
NIH Candidates Approved	2	3	1	2	4	3	1	2	2
Other Candidates	0	0	0	0	0	1	0	0	0
Invited	2	3	1	2	4	4	1	2	2
Declined	0	0	0	0	0	1	0	0	0
NIH Candidates Appointed	2	3	1	2	4	2	1	2	2
Other Candidates Appointed	0	0	0	0	0	1	0	0	0
Remaining Vacancies	0	0	0	0	0	0	0	0	0
Allergy Council									
Vacancies	2	2	2	2	2	2	4	3	4
NIH Candidates	6	5	4	4	4	6	7	6	6
NIH Candidates Approved	4	2	2	2	2	2	3	0	2
Other Candidates	0	0	0	0	0	0	0	1	0
Invited	4	2	2	2	2	2	3	1	2
Declined	2	0	0	0	0	0	0	0	1
NIH Candidates Appointed	2	2	2	2	2	2	3	0	1
Other Candidates Appointed	0	0	0	0	0	0	0	1	0
Remaining Vacancies	0	0	0	0	0	0	1	2	3
General Medical Sciences Council									
Vacancies	3	3	2	2	3	2	2	2	2
NIH Candidates	6	10	4	4	7	3	2	5	4
NIH Candidates Approved	5	5	2	2	3	1	1	2	2
Other Candidates	1	0	0	0	0	2	1	0	0
Invited	6	5	2	2	3	3	2	2	2
Declined	3	2	0	0	0	1	0	0	0
NIH Candidates Appointed	2	3	2	2	3	1	1	2	2
Other Candidates Appointed	1	0	0	0	0	1	1	0	0
Remaining Vacancies	0	0	0	0	0	0	0	0	0

	1965	1966	1967	1968	1969	1970	1971	1972	1973
Child Health Council									
Vacancies	2	2	2	2	2	3	3	2	2*
NIH Candidates	4	4	4	4	4	6	3	6	5
NIH Candidates Approved	2	2	2	2	2	3	1	1	0
Other Candidates	0	0	0	0	0	0	2	0	1
Invited	2	2	2	2	2	3	3	1	0
Declined	0	0	0	0	0	1	0	0	0
NIH Candidates Appointed	2	2	2	2	2	2	1	1	0
Other Candidates Appointed	0	0	0	0	0	0	2	0	0
Remaining Vacancies	0	0	0	0	0	1	0	1	2

* Pending since March 1973

	1965	1966	1967	1968	1969	1970	1971	1972	1973
Environmental Health Council									
Vacancies	ne	ne	ne	5	3	3	2	2	4
NIH Candidates	—	—	—	12	6	4	2	5	6
NIH Candidates Approved	—	—	—	5	3	3	1	0	3
Other Candidates	—	—	—	0	0	0	1	0	0
Invited	—	—	—	5	3	3	2	0	3
Declined	—	—	—	0	0	0	0	0	1
NIH Candidates Appointed	—	—	—	5	3	3	1	0	3
Other Candidates Appointed	—	—	—	0	0	0	1	0	0
Remaining Vacancies	—	—	—	0	0	0	0	2	2

ne = not in existence

	1965	1966	1967	1968	1969	1970	1971	1972	1973
Eye Council									
Vacancies	ne	ne	ne	ne	10	2	2	3	2
NIH Candidates	—	—	—	—	18	3	2	8	4
NIH Candidates Approved	—	—	—	—	10	1	1	2	1
Other Candidates	—	—	—	—	0	1	1	1	1
Invited	—	—	—	—	10	2	2	3	2
Declined	—	—	—	—	0	0	0	1	0
NIH Candidates Appointed	—	—	—	—	10	1	1	1	1
Other Candidates Appointed	—	—	—	—	0	1	1	1	1
Remaining Vacancies	—	—	—	—	0	0	0	1	0

ne = not in existence

	1965	1966	1967	1968	1969	1970	1971	1972	1973
Research Resources Council									
Vacancies	1	2	3	2	2	2	2	2	4
NIH Candidates	2	6	7	4	6	3	2	2	2
NIH Candidates Approved	1	3	4	2	2	2	2	0	2
Other Candidates	0	0	0	0	0	0	0	0	1
Invited	1	3	4	2	2	2	2	0	3
Declined	0	1	1	0	0	0	0	0	0
NIH Candidates Appointed	1	2	3	2	2	2	2	0	2
Other Candidates Appointed	0	0	0	0	0	0	0	0	1*
Remaining Vacancies	0	0	0	0	0	0	0	2	1

* Term begins 1/10/74

	1965	1966	1967	1968	1969	1970	1971	1972	1973*
Fogarty International Center Advisory Board									
Vacancies	ne	ne	ne	ne	ne	ne	ne	10	ne
NIH Candidates	--	--	--	--	--	--	--	10	--
NIH Candidates Approved	--	--	--	--	--	--	--	7	--
Other Candidates	--	--	--	--	--	--	--	3	--
Invited	--	--	--	--	--	--	--	10	--
Declined	--	--	--	--	--	--	--	1	--
NIH Candidates Appointed	--	--	--	--	--	--	--	6	--
Other Candidates Appointed	--	--	--	--	--	--	--	3	--
Remaining Vacancies	--	--	--	--	--	--	--	1	--

* Board abolished 3/30/73
ne = not in existence

	1965	1966	1967	1968	1969	1970	1971	1972	1973*
National Library of Medicine Board of Regents									
Vacancies	na*	na*	na*	3	2	1	3	3	5#
NIH Candidates	--	--	--	6	7	4	4	6	5
NIH Candidates Approved	--	--	--	3	2	1	1	0	0
Other Candidates	--	--	--	0	1	0	2	3	0
Invited	--	--	--	3	3	1	3	-**	0
Declined	--	--	--	0	1	0	0	-**	0
NIH Candidates Appointed	--	--	--	3	2	1	1	0	0
Other Candidates Appointed	--	--	--	0	0	0	2	0	0
Remaining Vacancies	--	--	--	0	0	0	0	3**	5

* Transferred from PHS to NIH on April 1, 1968.
** Action still pending as of 1/1/74. However, 2 OS candidates were confirmed by the Senate on 3/7/74.
# Includes 3 vacancies from previous year. The 5 NIH candidates are for the two 1973 vacancies.

Mr. Flood. Thank you very much.

APPROPRIATE AMOUNT OF FEDERAL SUPPORT FOR RESEARCH AND TRAINING

Mr. Michel. Dr. Stone, in the discussion here today you have referred to the question of what should be the appropriate amount of Federal support for research and training compared with outside support. Would you expand on that? How do you determine just what is the proper ratio, and do you feel this budget request approaches that mix?

Dr. Stone. Over the last two decades the NIH has assumed a relatively stable role relative to the amount of biomedical R. & D. and training that it supports and this is probably the most important element. If, for example, it were to become apparent that State support of State institutions of higher learning were being sharply curtailed and this was placing the NIH-sponsored research at these institutions in grave jeopardy, then certainly the NIH and the Federal role in general would need to be reevaluated but certainly a major responsibility of the NIH effort is to insure the stability of the research enterprise which is responsive to its needs as a health-research mission-oriented agency. It would be the NIH feeling that the budget request is certainly a responsible one in this regard.

NON-FEDERAL EXPENDITURES ON RESEARCH AND TRAINING

Mr. Michel. How do non-Federal expenditures on research and training now compare with Federal expenditures? Are they higher or lower than in the past? Last year you gave us some tables making this kind of comparison. Would you update those for us now?

Dr. Stone. Non-Federal sources continue to fund a substantial portion of the Nation's total biomedical research effort. During 1973 it was 37 percent. This support has remained at this level during the past decade.

[The information follows:]

National Support for Medical and Health Related Research and Development,

by Source of Support, 1947-1973 1/

(millions of dollars)

Year	Total	Federal	Non-Federal						
			Total	State and Local	Industry	Foundations & Health Agencies	Other Private Contribu-tions	Endowment	Institutions Own Funds
1973	$ 3,507	$ 2,206	$ 1,301	$ 80	$ 1,018	$ 116	$ 33	$ 19	$ 35
1972	3,352	2,145	1,207	79	925	116	33	19	35
1971	3,002	1,857	1,145	78	860	120	33	19	35
1970	2,728	1,664	1,064	76	795	108	32	19	34
1969	2,672	1,656	1,016	72	754	108	32	19	31
1968	2,486	1,571	915	69	661	106	30	19	30
1967	2,281	1,459	822	65	580	100	29	19	29
1966	2,053	1,316	737	61	510	91	28	19	28
1965	1,837	1,174	663	55	450	88	25	19	26
1964	1,652	1,049	603	50	400	88	22	19	24
1963	1,486	919	567	45	375	85	21	19	22
1962	1,290	782	508	37	336	78	18	19	20
1961	1,045	574	471	30	312	77	15	19	18
1960	845	448	397	23	253	76	12	19	14
1955	261	139	122	5	62	31	1	16	7
1950	161	73	88	-	51	21	N.A.	14	2
1947	87	27	60	N.A.	35	15	N.A.	10	N.A.

1/ Coverage is limited to conduct of research and development. Support of other activities such as research training or capital outlays for research facilities are not included.

Federal and Non-Federal Sources of Support for Medical and Health-Related Research and Development, 1947-1973[1]
(millions of dollars)

Fiscal Year	Amount			Percent of total		
	Total	Federal	Non-Federal	Total	Federal	Non-Federal
1973	$3,507	$2,206	$1,301	100%	63%	37%
1972	3,352	2,145	1,207	100	64	36
1971	3,002	1,857	1,145	100	62	38
1970	2,728	1,664	1,064	100	61	39
1969	2,672	1,656	1,017	100	62	38
1968	2,486	1,571	915	100	63	37
1967	2,281	1,459	822	100	64	36
1966	2,053	1,316	737	100	64	36
1965	1,837	1,174	663	100	64	36
1964	1,652	1,049	603	100	64	36
1963	1,486	919	567	100	62	38
1962	1,290	782	508	100	61	39
1961	1,045	574	471	100	55	45
1960	845	448	397	100	53	47
1955	261	139	122	100	53	46
1950	161	73	88	100	45	55
1947	87	27	60	100	31	69

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[1] Coverage is limited to conduct of research and development. Support of other activities such as research training or capital outlays for research facilities are not included.

Growth Rates of National Support for Performance of Medical and Health Related and Development, 1971-74 1/

Source of Funds	1971	1972	1973	1974 (est.)	1971/72	1972/73	1973/74 (est.)	1971/74 (est.)
	(million of dollars)				(growth rates)			
Total	$ 3,002	$ 3,352	$ 3,507	$ 4,117	11.7	4.6	17.4	37.1
Federal	1,857	2,145	2,206	2,733	15.5	2.8	23.9	47.2 2/
State & Local	78	79	80	84	1.3	1.3	5.0	7.7
Industry	860	925	1,018	1,095	7.6	10.1	7.6	27.3
Foundations and Health Agencies	120	116	116	118	-3.3	--	1.7	-1.7
Other	33	33	33	33	--	--	--	--
Endowments	19	19	19	19	--	--	--	--
Institutions' Own Funds	35	35	35	35	--	--	--	--

1/ Coverage is limited to conduct of research and development. Support of other activities such as research training or capital outlays for research facilities are not included.

2/ The high growth rate reflects inclusion of certain DHEW R&D funds withheld from FY 1973 appropriations and released in FY 1974. The FY 1971/1974 growth rate exclusive of such funds would have been 37 percent.

Mr. Michel. Where does this non-Federal support come from? What portion comes from the States? From industry? From foundations and private, nonprofit organizations? From gifts and donations?

Dr. Stone. In general certainly a substantial portions comes from the States. The proportion which comes from industry has been remarkably stable over a number of years and during this time has represented a proportion of R. & D. excluding training and facilities that represents a little less than one-third both by performer and by source, indicating that industry essentially takes the money out of one pocket and puts in the other. The amounts from foundations and other organizations of this kind is relatively small, accounting for less than 10 percent.

SHIFT TO DIRECT SUPPORT OF INDIVIDUALS IN RESEARCH TRAINING

Mr. Michel. Have you taken a close, hard look at the actual effect on the budgets of institutions, of the shift to direct support of the individual in research training? Do you have any really hard information as to what this will mean to them in terms of actual dollars?

Dr. Stone. If, over a period of time, the proportionalities instituted by the new NIH research manpower and development program are continued as the old training grants and fellowships are phased out, there would be some decrease in the actual dollars going to institutions in connection with NIH research training support. The proportion of training funds would shift from a little less than half going toward the support of institutional resources to about a third.

Mr. Michel. This whole approach of support to the individual rather than to the institution directly, has been taken by the administration in the field of higher education. Do you really feel it is an appropriate approach in the area of research training? A part of the idea is to allow the individual to "shop around" for the institutions with the strongest programs, or the programs best suited for him, isn't it? But, is this really practical where research training is concerned?

Dr. Stone. NIH has always provided substantial opportunities for individuals to seek fellowship support and to seek out the institutions most suited to their needs. At the same time, however, it has always insisted on a careful evaluation in connection with the competitive application of the appropriateness of the institutional setting for the research training proposed. Providing the review of applications encompasses this important element of the quality of the research training environment, we see no difficulties in allowing the candidate to select his institution. The new Fellowship program does provide for a limited number of "institutional" awards so that there will continue to be a mix of approaches to support, et cetera.

CONTRACTS

Mr. Conte. On how many contracts do NIH intramural staff serve as project officers? What is the total dollar amount of those contracts? How many of these contracts were sole source contracts?

Dr. Stone. Members of the intramural NIH staff serve as contract officers on 434 contracts of which 186 are sole source contracts. The total dollar value of these 434 contracts is $59.9 million.

Mr. Conte. For the record, could you break down by disease areas the increased contract funds requested for 1975?

Dr. Stone. Yes sir.

[The information requested follows:]

Fiscal year 1975 increases in contract funds for specific disease areas

NCI: Immunology	$125,000
NHLI:	
Heart and vascular disease	2,450,000
Research in lung disease	515,000
Research related to blood diseases and blood resources	1,490,000
NIAMDD:	
Arthritis	550,000
Skin diseases	100,000
Diabetes	200,000
Endocrinology	300,000
Digestive diseases	400,000
Kidney diseases	201,000
Hematology	50,000
NINDS:	
Epilepsy	400,000
Stroke and head injury	300,000
Multiple sclerosis	250,000
Communicative disorders	150,000
Parkinson's disease	60,000
NIAID:	
Allergic reagents	84,000
Venereal disease	355,000
Diseases preventable by vaccines	45,000
Mycrobacterial disease	50,000
Influenza and selected respiratory diseases	600,000
Viral hepatitis	250,000
Rabies	16,000
NICHD:	
Population	1,199,000
Child health	186,000
Aging	135,000
NEI:	
Corneal disease	50,000
Glaucoma	150,000

MULTIYEAR FUNDING

Mr. Conte. Have all of the "released" 1973 funds been used for multiyear funding of projects? What is the total number of projects funded from released 1973 funds? If multiyear funding had not been used, and taking as a base the average annual award, how many projects could have been started with those released funds?

Dr. Stone. By and large, the released 1973 funds were not used for multiyear funding. Due to the timing of the release of these funds, a number of training grants were made for periods longer than 12 months so that they could be brought into line with the academic year. The duration of these grants is mostly between 12 and 18 months—in any event, less than 2 years—and we do not regard that as multiyear funding. Among the research grants there are always some that are awarded for more than 1 year, for various special reasons related to the nature of the project. Of the total of $1,199 million available in fiscal year 1973, before the release of the impounded funds, for fellowships, training grants, research grants and contracts, about $16.9 million was used for multiyear awards. That is less than 1½ percent. The court ordered that the released funds should be spent in the same pattern as if they had been available in 1973. Out of the additional $219 million made available less than 1 million—$935,000 actually—was used for multiyear grants. That is less than ½ percent. There has certainly been no policy to encourage multiyear funding. In fact, we have actively discouraged it.

The total number of projects funded from 1973 released funds was 2.273 including 290 research contracts and 27 projects funded by the National Library of Medicine. That number might have been increased by no more than 20 if there had been no multiyear funding at all.

UNFUNDED GRANT APPLICATIONS

Mr. Conte. How many approved grant requests for 1973 were turned down because of lack of funds? How many of those were from young investigators or first-time applicants?

Dr. Stone. We had 4,444 approved grant applications for fiscal year 1973 for which awards could not be made because no further funds were available. I cannot give you a complete answer for the second part of your question because three of the Institutes do not have this information available. For the others, the number of first-time applicants who had approved but unfunded grant applications was 789. For NIH as a whole the figure would be close to 1,000. In other words, between a fifth and a quarter of the unfunded grant applications were from first-time applicants.

PRIORITY CUT-OFF FUNDING POINTS

Mr. Conte. Your reviewers assign priorities to projects they approve. Will you provide for the record, by Institute, the priority cutoff for funding for fiscal years 1972. 1973 and the estimated cutoffs for 1974 and 1975?

Dr. Stone. Yes sir. As you know, priority scores range from 100—the highest score possible—to 500 which is the lowest. This applies only to projects regarded as meritorious and worthy of support. Grant applications that are disapproved do not get a priority score. The median score is thus 300. For purposes of payment, the grant applications for each Institute, or program area, are arranged in priority order and payment, in general, is made from the top down. The cutoff point, where the money runs out, for most of the Institutes is in the 200's though it is even higher than that—say, 180 or 190—for a few. We will supply a table for the record.

[The information requested follows:]

PRIORITY CUT-OFF POINTS FOR FUNDING RESEARCH GRANTS

Institute	1972	1973	1974 (estimate)	1975 (estimate)
NCI	286	256	265	200
NHLI	267	242	260	250
NIDR	279	291	253	220
NIAMDD				
NINDS	225	225	250	215
NIAID	232	235	220	185
NIGMS	235	208	205	185
NICHD	280	207	286	200
NEI	261	241	250	220
NIEHS	243	280	210	190
RR	333	275	291	275
FIC	340	366	350	250
NLM	350	293	291	303

RESEARCH CAREER AWARDS

Mr. Conte. You're phasing out the research career program. How many full-time research appointments are there in schools of medicine that are not supported by that program?

Dr. Stone. We are not phasing out the research career program—we have simply moved it from the training rubric in the budget to the research rubric where it really belongs. We have not made any research career awards for a number of years, as the result of an NIH policy decision, but we are honoring the commitments that had already been made. The research career development awards, given to somewhat younger people and limited to 5 years, are still being made and will continue to be made. But the funds for both of these programs are now included in the research, rather than the training, part of the budget.

I do not know how many full-time research people there are in medical schools. The typical pattern among medical school faculty is to combine research with teaching and patient care—and, to some extent administrative duties, especially among the senior people. The distribution of effort varied markedly, from school to school and among faculty members. And in clinical research it is, of course, not possible to draw a line between time spent on research and time spent on patient care. In most medical schools and large urban hospitals there are people whose prime interest and responsibility is a large research program which, incidentally, takes care of a lot of patients. I don't know whether one should call them full-time research people and, in any case, I don't know many there are. The number of full-time research appointments—that is, people hired specifically to do nothing but research—is very much smaller but, again, it is hard to draw the line. For example, all the intramural physicians who take care of patients in our clinical center were hired to do full-time research. Similar situations exist in medical schools and research hospitals.

Mr. Conte. How much was awarded in 1973 for salaries for career investigators?

Dr. Stone. Awards under our research career awards program in 1973 totaled $25.9 million. Of this amount about $22.4 million was for salaries. There were 1,088 awards in the research career and research career development programs.

Mr. Conte. If funds have to come from research grants to keep these people in business, what proportion of funds otherwise available for new grants would be needed?

Dr. STONE. The funds for research career and research career development awards are built into the budget—whether they are included under the fellowships and training heading, as heretofore, or under the research grant heading as at present, is really a technical detail. It is a little more realistic to include funds for people doing full-time research under the research grant heading. If the $25.9 million spent on these awards had been available for regular research grants an additional 375 grants awards could have been made—but that would be true of the availability of an additional $25.9 million from any source. That amount is equivalent to about 10 percent of the funds available for competing research projects.

GENERAL RESEARCH SUPPORT GRANTS

Mr. CONTE. What have been the major uses of general research support grants?

Dr. STONE. The general research support funds may be, and have been, used for generally the same types of expenditures as the regular research project grant funds but in a flexible manner as determined by the grantee institution. For example, they may be used for the payment of salaries, purchase of equipment, patient care costs, and travel. These expenditures generally fall into two major areas; the first is the support of research projects including pilot projects by young investigators, and also for the provision of central resources such as animal facilities, computer facilities, general use equipment, and central laboratory facilities. In 1972, 68 percent of the total funds expended went toward the support of approximately 7,800 research projects covering over 100 diverse scientific disciplines in the biomedical sciences. The majority of these funds support studies in neurological diseases, endocrinological and cardiovascular problems, infections and parasitic conditions, metabolic disorders, immunology and allergy, pharmacological research, and biochemistry.

EARLY RETIREMENT

Mr. CONTE. For each Institute, how many scientific personnel, grade 15 and above, have resigned or taken early retirement in 1973 and 1974?

Dr. STONE. I'll be glad to supply that for the record.

[The information requested follows:]

NUMBER OF SCIENTIFIC PERSONNEL GS-15 AND ABOVE WHO HAVE RESIGNED OR TAKEN EARLY RETIREMENT

Institute/Division	1973	1974
NCI	7	8
NHLI	1	1
NINDS	2	1
NIAID	2	2
NICHD	7	1
NLM	1	0
Total	20	13

Mr. Robinson. With respect to the plan to emphasize competitive fellowships in the future support of research training programs, and to phase out training grants, I should like you to comment on why you believe—if you do—that this will not diminish the infusion of new blood, so to speak, in medical research. Do you see any validity to the criticism, which I believe has been made, that the emphasis on postdoctoral fellowships is not conducive to the training of new researchers but, rather, a bonus for committed and trained researchers? Additionally, is there any basis, in your view, for a fear that the structure of the competitive selection process might contribute to a concentration of research effort control and inhibit the imaginative efforts of independent research centers?

Dr. Stone. Let me answer these questions in a different order—dealing first with the allegation that postdoctoral fellowships are a bonus for researchers who are already trained. This is simply not the case. Most of the postdoctoral fellowships are awarded to those who have just earned an MD degree. While medical students are, these days, exposed to a fair amount of research and while some of them may have participated in a research project, they have not, in any practical sense, been trained in research in the way that, say, a Ph. D. candidate in biochemistry is trained in research. The medical school curriculum is already too crowded and, in the opinion of many, already ignores, for want of time, some things that ought to be more thoroughly covered. The new MD wishing to go into research must therefore be trained after he has received his medical degree. In our definition, that is postdoctoral training.

Postdoctoral fellowships are also awarded to those who already have a Ph. D. and have thus already had research training and experience. In these cases, however, the purpose of the grant is to enable the fellow to work with a particular investigator who is at the forefront of research in some specialized field or to enable him to join a team of researchers at some highly specialized facility. He is, so to speak, receiving advanced research training. He is certainly not receiving this kind of fellowship support merely to do what he was doing anyway.

I see no reason for believing that substituting fellowship support for training grant support will significantly diminish the flow of new blood into research. It may be a little more difficult for some aspiring researchers to obtain a fellowship in national competition than to gain acceptance in a local training program but, in general, I do not think that the mechanisms of support are a major factor if the volume of support available remains roughly the same. We must also not overlook the possibility—I should say, probability—that opportunities for research training will remain open to bright young people at the local level.

Nor do I think that the competitive selection process that is an essential part of the fellowship program will restrict or inhibit imaginative research. All the people involved in the selection process are very strong supporters of the view that first-class research cannot be preplanned by others. They are staunch defenders of the inherent necessity, given the nature of biomedical research, for complete independence to follow leads, exploring side issues, and to pursue unexpected opportunities. Fellows will be selected on the basis of their demonstrated competence and promise for future development and they will remain free to follow their own professional course and pursue their own scientific interests. They are in no sense being hired to do a job defined by somebody else.

On the other hand, I think that it is important to point out that these postdoctoral fellows are really doing a job—a very important job. They devote their full time to doing research. They are not in a passive training situation. They do not just stand around watching somebody else doing research. They are deeply immersed in serious research projects and they are solving problems and making contributions to knowledge—just like any other research investigator. It is very much a case of on-the-job training. The training is important to the fellow's development as an investigator but we should not forget that the job he is doing also needs to be done and may, indeed, result in very important advances in his field of science.

A switch from training grants to fellowships will have a noticeable impact on the institutions, or the departments, that have provided training in the past because training grants have, in a way, been a form of institutional or departmental support. It should not, however, be an impediment to those seeking training. On the contrary, a fellow has a degree of flexibility and independence, especially in choosing the place at which he wishes to work, that a trainee under a training program does not have.

Mr. Flood. Thank you very much.

Tuesday, March 26, 1974.

NATIONAL CANCER INSTITUTE

WITNESSES

DR. FRANK J. RAUSCHER, JR., DIRECTOR

DR. ROBERT S. STONE, DIRECTOR, NATIONAL INSTITUTES OF HEALTH

DR. DeWITT STETTEN, JR., DEPUTY DIRECTOR FOR SCIENCE, NATIONAL INSTITUTES OF HEALTH

DR. BAYARD H. MORRISON III, ASSISTANT DIRECTOR, NATIONAL CANCER INSTITUTE

CALVIN B. BALDWIN, JR., EXECUTIVE OFFICER, NATIONAL CANCER INSTITUTE

EARLE L. BROWNING, FINANCIAL MANAGER, NATIONAL CANCER INSTITUTE

LEON M. SCHWARTZ, ASSOCIATE DIRECTOR FOR ADMINISTRATION, NATIONAL INSTITUTES OF HEALTH

LELAND B. MAY, ACTING DIRECTOR OF FINANCIAL MANAGEMENT, NATIONAL INSTITUTES OF HEALTH

CHARLES MILLER, DEPUTY ASSISTANT SECRETARY, BUDGET

Object Classification (in thousands of dollars)

Identification code 09–25–0849–0–1–651		1973 actual	1974 est.	1975 est.
	Direct obligations:			
	Personnel compensation:			
11.1	Permanent positions	25,563	29,265	31,278
11.3	Positions other than permanent	1,250	1,505	1,585
11.5	Other personnel compensation	677	859	885
	Total personnel compensation	27,490	31,629	33,748
12.1	Personnel benefits: Civilian	3,185	3,537	3,750
21.0	Travel and transportation of persons	1,776	2,150	2,200
22.0	Transportation of things	293	335	340
23.0	Rent, communications, and utilities	1,533	1,800	2,200
24.0	Printing and reproduction	741	900	950
25.0	Other services	169,542	247,175	253,399
26.0	Supplies and materials	10,113	12,000	13,200
31.0	Equipment	2,542	3,900	4,000
41.0	Grants, subsidies, and contributions	214,030	285,729	286,213
	Total direct obligations	431,245	589,155	600,000
	Reimbursable obligations:			
21.0	Travel and transportation of persons	3	6	6
25.0	Other services	23	25	25
	Total reimbursable obligations	26	31	31
99.0	Total obligations	431,271	589,186	600,031

Personnel Summary

	1973 actual	1974 est.	1975 est.
Total number of permanent positions	1,736	1,844	1,873
Full-time equivalent of other positions	129	156	165
Average paid employment	1,850	1,955	2,011
Average GS grade	8.5	8.6	8.6
Average GS salary	$14,260	$15,138	$15,473
Average salary of ungraded positions	$11,138	$12,018	$11,253

Program and Financing (in thousands of dollars)

Identification code 09–25–0849–0–1–651	1973 actual	1974 est.	1975 est.
Program by activities:			
Direct program:			
1. Research:			
(a) Cause and prevention research	106,095	145,778	151,662
(b) Detection, and diagnosis research	22,539	40,264	43,244
(c) Treatment research	122,353	193,862	205,128
(d) Cancer biology	47,708	84,798	89,821
Total research	298,695	464,702	489,855
2. Resource development:			
(a) Cancer centers support	11,124	20,334	23,484
(b) Research manpower development	18,509	18,530	18,530
(c) Construction	25,696	50,990	22,317
Total resource development	55,329	89,854	64,331

Program and Financing (in thousands of dollars)

	Identification code 09–25–0849–0–1–651	1973 actual	1974 est.	1975 est.
	3. Cancer control:			
	(a) Cancer control	376	34,599	45,814
	Total direct program	354,400	589,155	600,000
	Reimbursable program: Treatment research	26	31	31
	Total program costs, funded [1]	354,426	589,186	600,031
	Change in selected resources (undelivered orders)	76,845		
10	Total obligations	431,271	589,186	600,031
	Financing:			
	Receipts and reimbursements from:			
11	Federal funds	−23	−25	−25
14	Non-Federal sources	−3	−6	−6
17	Recovery of prior year obligations	−892		
21	Unobligated balance available, start of year	−307	−61,849	
24	Unobligated balance available, end of year	61,849		
25	Unobligated balance lapsing	355		
	Budget authority	**492,250**	**527,306**	**600,000**
	Budget authority:			
40	Appropriation	492,205	551,192	600,000
	Withheld from obligation and expenditure (Public Law 93–192)		−23,706	
41	Transferred to other accounts		−180	
42	Transferred from other accounts	45		
43	Appropriation (adjusted)	492,250	527,306	600,000
	Relation of obligations to outlays:			
71	Obligations incurred, net	430,353	589,155	600,000
72	Obligated balance, start of year	273,296	319,339	377,496
74	Obligated balance, end of year	−319,339	−377,496	−418,085
90	Outlays	384,310	530,998	559,411

[1] Includes capital outlay as follows: 1973, $2,542 thousand; 1974, $3,900 thousand; 1975, $4,000 thousand.

NOTES

Includes $333 thousand in 1975 for activities previously financed from (in thousands of dollars):

	1975
National Institute of General Medical Sciences	326
Departmental Management	7

Comparable amounts for 1973 ($286 thousand) and 1974 ($286 thousand) are included above.

Excludes $180 thousand in 1974 and 1975 for activities transferred to Departmental Management. Comparable amount for 1973 ($180 thousand) is included above.

Excludes $193 thousand in 1975 for activities transferred to: Office of Assistant Secretary for Health. Comparable amounts for 1973 ($193 thousand) and 1974 ($193 thousand) are included above.

Mr. FLOOD. The committee will come to order.

Now we have the National Cancer Institute. The presentation will be made by Dr. Frank J. Rauscher, Director. We have a biographical sketch of Dr. Rauscher we will place in the record.

[The biographical sketch follows:]

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE—PUBLIC HEALTH SERVICE, NATIONAL INSTITUTES OF HEALTH, NATIONAL CANCER INSTITUTE

BIOGRAPHICAL SKETCH

Name.—Frank J. Rauscher, Jr., Ph. D.

Position.—Director, National Cancer Program, National Cancer Institute.

Birthplace and date.—Hellertown, Pa., May 24, 1931.

Education.—Moravian College, Bethlehem, Pa., 1953, B.S. premedical curriculum; Ph. D., Rutgers, The State University, New Brunswick, N.J., June 1957.

Experience.—Present Director, National Cancer Program, National Cancer Institute; 1970–72, scientific director for etiology, NCI; 1969–70, acting scientific director for etiology, NCI; 1967–70, associate scientific director for viral oncology, etiology, NCI; 1966–67, chief, viral leukemia and lymphoma branch, etiology, NCI; 1965–66, acting chief, viral leukemia and lymphoma branch, etiology, NCI; 1964–70, chairman, special virus (leukemia) cancer program, etiology, NCI; 1964–66, head, viral oncology section, laboratory of viral oncology, NCI; 1962–67, visiting investigator of viral oncology, Rutgers University; 1959–64, microbiologist, National Cancer Institute, laboratory of viral oncology; 1959– , visiting instructor of animal virology, Trinity College, Washington, D.C.; 1958–59, assistant professor of virology, Rutgers University graduate school, New Brunswick, N.J.; 1957–58, research associate in virology, Rutgers University graduate school, New Brunswick, N.J.; 1955–57, research assistant in virology, Rutgers University graduate school, New Brunswick, N.J.; 1953–55, research fellow in virology, Rutgers University graduate school, New Brunswick, N.J.

Association memberships.—The Theobald Smith Society, N.J., Society of Sigma Xi, the American Association for Cancer Research, the American Association of Immunologists, the American Association for Advancement of Science, World Society for Leukemia and Related Diseases.

Special awards, citations, or publications.—Comenius Awards—presented annually by Moravian College, Bethlehem, Pa., to a person "for outstanding scientific achievement." April 1963. U.S. Junior Chamber of Commerce Award—presented to the Nation's ten outstanding young men." January 1965, Selman A. Waksman honorary lectureship award—presented annually by the Theobald Smith Society, the New Jersey branch of the American Society for Microbiology for "Outstanding contributions to microbiology." March 1967. Arthur S. Flemming award—presented annually to the "ten outstanding young men in the Federal Government." February 1968. Vice president, World Society for Comparative Leukemia Research, 1967–72. Elected to board of directors, American Association for Concer Research, 1970. Elected—board of trustees, April 1970, of Moravian College, Bethlehem, Pa., for the period 1971–74. Appointment—International Agency for Research on Cancer; member of scientific council, 1972– ; chairman, U.S. Delegation, governing council, 1972. Distinguished Service Award—presented by the Department of Health, Education, and Welfare, July 1972. And 52 publications on virology, cancer research, cancer planning, and biomedical management.

Mr. FLOOD. Do you have anybody with you you would like to introduce?

Dr. RAUSCHER. Thank you, Mr. Chairman.

I have with me our executive officer, Mr. Calvin Baldwin, and financial manager, Mr. Earle Browning. You, of course, know Dr. Stone, our Director.

Mr. FLOOD. I see you have a prepared statement.

Dr. **Rauscher**. Thank you, Mr. Chairman. I would like to read it into the record if I may.

Mr. **Flood**. You may proceed.

OPENING STATEMENT

Dr. **Rauscher**. Mr. Chairman, and members of the committee: I appear before the committee today to report on the national cancer program and our efforts to control cancers in people. Mr. Chairman, in terms of public health impact, 1,000 Americans die every day with the more than 100 diseases we call cancer. This is our task and opportunity.

The National Cancer Act of 1971 authorized the National Cancer Institute to carry out a broad and coordinated effort against cancer. The national cancer program will discover and develop means for the prevention of cancer, the cure of cancer when it occurs, and the restoration of former cancer patients to productive lives.

COORDINATION OF ACTIVITIES

The national program—it is in fact international in scope—includes activities at the other National Institutes of Health and 12 other Federal agencies. It includes the activities of universities, hospitals, research institutes, industrial firms, and voluntary organizations such as the American Cancer Society.

STRATEGIC PLAN

Coordination of the program is guided by a strategic plan of research approaches for progress toward the program's goals. The strategic plan was transmitted to the Congress by the President last year. The plan was developed with the advice of eminent members of the scientific community. The plan has already been updated early this year, and will be kept current with continuing advice from scientists and physicians.

BUDGET FORMAT

You have before you the proposed budget for fiscal 1975. This is the first time that our budget has been presented by describing the major research thrusts related to the disease process. These are cancer cause and prevention, cancer detection and diagnosis, cancer treatment, and cancer biology. We believe that this is a more informative presentation of how public funds are being spent. The traditional budget categories are also presented.

The accompanying budget justifications set forth the research challenges in each research area and the approaches to deal with each. The justification also describes the accomplishments under the national cancer program during fiscal year 1974 and new activities planned for 1975. I will now present some of the highlights.

The national cancer program has a dual mission: the development of new knowledge through research and the delivery of research results to people through demonstrations of the best of our present knowledge. Before turning to research findings, I would like to inform you of progress in direct people benefit through two major programs: cancer control and comprehensive cancer centers.

CANCER CONTROL

The cancer control program is a primary channel for rapidly moving research results into community medical practice including cancer centers, community hospitals, State health departments, voluntary agencies and other organizations.

In cooperation with the American Cancer Society, 27 demonstration projects for the early detection of breast cancer have been established throughout the country. Mr. Chairman, I would like to enter into the record the locations of these detection projects.

Mr. Flood. Without objection we will do that.

[The information follows:]

BREAST CANCER DEMONSTRATION PROJECTS

East:
- Guttman Institute, New York, N.Y.
- College of Medicine and Dentistry of New Jersey, Newark, N.J.
- University of Pittsburgh, School of Medicine, Pittsburgh, Pa.
- Albert Einstein Medical Center, Philadelphia, Pa.
- Wilmington Medical Center, Wilmington, Del.
- Rhode Island Hospital, Rhode Island Department of Health, Providence, R.I.

South:
- University of Louisville, School of Medicine, Louisville, Ky.
- St. Vincent's Medical Center, Jacksonville, Fla.
- Duke University Medical Center, Durham, N.C.
- Emory University—Georgia Baptist Hospital, Atlanta, Ga.
- Georgetown University Medical School, Washington, D.C.
- Vanderbilt University, School of Medicine, Nashville, Tenn.

Midwest:
- University of Kansas Medical Center, Kansas City, Kans.
- Medical College of Wisconsin, Milwaukee, Wis.
- University of Cincinnati Medical Center, Cincinnati, Ohio.
- Iowa Lutheran Hospital, Des Moines, Iowa.
- University of Michigan Medical Center, Ann Arbor, Mich.
- Ellis Fischel State Cancer Hospital, Columbia, Mo.
- University of Arizona, Arizona Medical Center, Tucson, Ariz.

West:
- University of Oklahoma, Health Sciences Center, Oklahoma City, Okla.
- Mountain States Tumor Institute, Boise, Idaho.
- Virginia Mason Research Center, Seattle, Wash.
- Pacific Health Research Institute, Inc., Honolulu, Hawaii.
- Samuel Merritt Hospital, Oakland, Calif.
- University of Southern California, Los Angeles, Calif.
- Good Samaritan Hospital and Medical Center, Portland, Oreg.
- St. Joseph's Hospital, Houston, Tex.

Dr. Rauscher. Seven regional networks of community hospitals and individual physicians are being established to demonstrate the most effective treatments for childhood acute leukemia and for Hodgkin's disease and other lymphomas.

Three projects have been started for the early detection and treatment of lung cancer in persons at high risk—men 45 to 69 years of age who are regular cigarette smokers.

Seven projects are demonstrating the rehabilitation of cancer patients through improved practices in physical therapy, occupational therapy, and restoration of acceptable appearance and functions.

New projects planned for 1975 include efforts in the control of environmental hazards, particularly in the workplace. Other projects will be directed toward the reduction of lung cancer and early detection of cancer of the cervix and of the colon.

COMPREHENSIVE CANCER CENTERS

The program of cancer centers bridges the twin missions of research and demonstration. Research at a comprehensive cancer center covers basic and clinical studies. They also train manpower to meet present and future needs of the national cancer program.

Further, they demonstrate to health practitioners and other institutions in their surrounding areas the best programs of cancer prevention, detection, diagnosis, treatment and rehabilitation. Although comprehensive centers are not a medical delivery system, their demonstration and outreach programs will exert a significant impact on the quality of cancer care throughout the Nation.

When, in 1971, the National Cancer Act authorized the establishment of new comprehensive cancer centers, there were three preexisting centers: The M. D. Anderson Hospital and Tumor Institute, Houston; Memorial Sloan-Kettering Cancer Center, New York City; and Roswell Park Memorial Institute, Buffalo.

There are now 12 comprehensive cancer centers across the United States. Mr. Chairman, I would like to submit for the record a list of these centers.

Mr. FLOOD. Without objection, that will be done.

[The information follows:]

COMPREHENSIVE CANCER CENTERS

1. M. D. Anderson Hospital and Tumor Institute, Houston.
2. Memorial Sloan-Kettering Cancer Center, New York.
3. Roswell Park Memorial Institute, Buffalo.
4. Children's Cancer Research Foundation, Boston.
5. The Johns Hopkins Medical Institutions, Baltimore.
6. Duke University Medical Center, Durham, N.C.
7. University of Alabama School of Medicine, Birmingham.
8. University of Wisconsin Medical Center, Madison.
9. Fred Hutchinson Cancer Research Center affiliated with the University of Washington, Seattle.
10. University of Southern California (with the Los Angeles County Department of Hospitals), Los Angeles.
11. University of Miami School of Medicine, Miami.
12. Mayo Foundation, Rochester, Minn.

Dr. RAUSCHER. Before the end of this fiscal year, we expect to designate four to six additional centers, bringing more than 100 million Americans within 60 miles of one of these institutions.

We are beginning additional approaches to the regional outreach of cancer centers. The first community cancer center, the Mountain States Tumor Institute, has been established in Boise, Idaho, in affiliation with the Fred Hutchinson Cancer Research Center in Seattle, Wash. This institute should serve as a prototype for translating research findings into clinical practice in other communities which do not have a medical school. Planning activities are underway for community cancer centers in other areas, and we expect that several will be operational soon.

CANCER CAUSE AND PREVENTION

I would now like to turn to the research thrusts of the national cancer program. Studies across a very broad front are yielding new insights into how cancer may be avoided and how the treatment of cancer may succeed even better.

Although cancer once was thought to arise from inborn defects, we now believe that external factors are responsible for up to 90 percent of cancer cases. The identification of such factors thus will help us prevent these diseases.

The National Cancer Institute currently is testing approximately 450 chemicals—including industrial compounds, pesticides, food additives, and drugs—in 2-year to 3-year studies with animals. These tests are underway at 20 laboratories, including the Frederick Cancer Research Center at Fort Detrick, Md. At the same time, scientists are continuing to make progress toward a rapid and less expensive screening test for chemicals with cancer-causing activity.

No virus has yet been proven to cause human cancer, but scientists continue to accumulate evidence for association of viruses with breast cancer, leukemia, cancer of the cervix, and other forms of cancer. Other scientists are looking for ways in which viruses and chemicals may act in concert to cause cancer. An understanding of these processes at a molecular level may lead to the means to block the cancerous transformation or to prevent it.

Studies of human population groups can provide evidence for causes of cancer or identify people that are especially susceptible to developing cancer. Of particular concern currently are the results of a study reported last year that indicates an alarming increase in cancer among U.S. black men. The cancer death rate for black men in the United States increased 50 percent from 1950 to 1967, as compared with a 16-percent increase for white men.

To gather and analyze cancer statistics on a yearly basis, the National Cancer Institute in 1973 began a program called the cancer surveillance, epidemiology, and end results reporting, or SEER program. This will provide a steady flow of information on new cancer cases and their variation among population groups and geographic areas. SEER also will pinpoint increases in survival rates of cancer patients as related to changes in diagnostic and treatment practices.

DETECTION AND DIAGNOSIS

Research on cancer detection and diagnosis is to find cancer at its earliest stages, when it is most readily cured. We now have convincing evidence, for example, that earlier detection of breast cancer can lead to recovery from that disease for a greater number of women.

Research and demonstration programs are continuing to exploit the use of cell samples for cancer detection. The Pap test has had a major impact on reducing the death rate from cervical cancer in this country. A test similar to the Pap test can detect lung cancer earlier through analysis of cells in sputum samples. Other cell tests may be useful in screening for bladder cancer and several other cancers.

Immunologic reactions are also opening up new leads in cancer detection and diagnosis, particularly for following the progress of therapy. Studies by NCI and other institutions have resulted in licensing by the Food and Drug Administration of a test for carcinoembryonic antigen, commonly referred to as CEA. CEA occurs in the bloodstream in association with a number of forms of cancer, including cancer of the colon.

Other NCI scientists have developed a highly sensitive immunologic test for alphafetoprotein, or AFP. Again, this test seems to be most useful in following the response of certain cancer patients to treatment, especially when AFP and CEA or other factors are measured together.

TREATMENT

Progress is continuing in more effective combinations of surgery, radiation, and drugs in the treatment of cancer. At the same time, scientists are exploring the possibilities of immunotherapy as a fourth mode for combination therapy. We are particularly focusing treatment research on the solid tumors, including cancers of the lung, breast, and colon—the biggest cancer killers in this country.

Radiation and a combination of three anticancer drugs have produced improvement in patients with small cell carcinoma of the lung. This is a relatively rare form of lung cancer, but also one of the most rapidly lethal forms of this disease.

Drug treatments for advanced breast cancer recurring after surgery are under study at a number of institutions. The studies have begun too recently to know whether survival rates will be improved, but drug combinations have already produced a complete disappearance of cancer symptoms in some of the patients.

More than 47,000 substances were screened for anticancer activity last year and 15 compounds passed NCI's stringent tests in animals and were accepted for use in cancer patients.

We are expanding research with high-energy neutrons and negative pi mesons in radiotherapy. These subatomic particles are potentially capable of killing cancer cells deep within much larger tumors, while being less damaging to surrounding normal tissue than are the X-rays and gamma-rays used at present.

CANCER BIOLOGY

Research in cancer biology provides fundamental information on the cancerous process at a cellular and molecular level. Within the definitions used in the preparation of this budget, cancer biology refers to basic research that is potentially applicable to all of the other research thrusts but cannot be classified with any single thrust. In this same sense, a greater understanding of this mysterious disease process may also come from research conducted by other of the National Institutes of Health.

Immunologic methods of treatment and diagnosis are just beginning to emerge from basic research on the components and mechanisms of the immune system. We expect that other totally new approaches for cancer control and prevention will eventually be discovered.

Scientists are probing changes in genetic controls, cell enzymes and cell membranes that occur when normal cells become cancerous. An artificial and potentially functioning gene has been synthesized for the first time. Artificial genes may serve as experimental systems for the study of how cells multiply—and how their multiplication can be stopped.

Hybrid cells formed by fusing cancer cells with normal cells or other cancer cells are also revealing properties of cancer cells that may be used to destroy them or even return them to normal.

MANPOWER AND CONSTRUCTION

The effective expansion of the national cancer program depends on adequate manpower and physical facilities. The program of fellowships and graduate and clinical training grants will be restored. A new clinical education program will make awards to medical schools for the creation of innovative education programs.

Construction during the present year includes eight projects, four of them at Comprehensive Cancer Centers. Construction during fiscal 1975 may be limited to modernization and renovation of existing facilities, including cancer research centers and facilities on the NIH campus and at the Frederick Cancer Research Center.

The conquest of cancer is a long-term objective. We are still exploring vast, uncharted areas of biology and medicine. Even so, we are vigorously attempting to come to grips with what we do not understand and to apply what we already know. It will probably take years to begin to achieve dramatic results, although each life saved or prolonged is a real victory.

On balance, we are making progress, and we will continue to do so. Although an estimated 655,000 Americans will develop cancer in 1974, and 355,000 will lose their lives, there are 1½ million who have had cancer but are now well. An additional 1 million cancer patients diagnosed and treated in the last 5 years are expected to live to join these ranks. An increasing number of them will have had cancers recently thought to be incurable.

APPROPRIATION REQUEST

Mr. Chairman, the request for the National Cancer Institute totals $600 million, an increase of $69,611,000 over the 1974 base obligations of $530,389,000. The new request includes increases of $18,181,000 for cause and prevention research, $4,495,000 for detection and diagnosis research; $24,454,000 for treatment research; $11,833,000 for cancer biology; $3,906,000 for cancer centers support; $4 million for research manpower development; and $11,215,000 for cancer control. There is a decrease of $8,473,000 in construction activities.

I shall be pleased to try to answer any questions and supply additional information desired for the record.

Mr. Chairman, this concludes my statement.

DEATH RATE FROM CANCER

Mr. Flood. Doctor, is the death rate from cancer continuing to rise?

Dr. Rauscher. The number of new cases is continuing to rise. The death rate in many of our cancers like colon and lung continue to rise. However, in others it is practically level. Acute lymphocytic leukemia of children is decreasing, stomach cancer is decreasing.

Mr. Flood. What type of cancer kills most people?

Dr. Rauscher. Lung cancer, colon, and breast.

Mr. Flood. For the record we are going to want a lot of things today. Give us for the record the statistics on the death rate and the number of deaths from various types of cancer, along with similar statistics now and for a certain number of previous years.

[The information follows:]

STATISTICS ON DEATH RATES AND NUMBER OF DEATHS FOR VARIOUS TYPES OF CANCER

[Latest available data regarding the death rates and number of deaths for various types of cancer. Rates are based on total U.S. population in 1960 and are per 100,000 population (age adjusted[1]) for the period 1950–69. These rates are for the 48 contiguous United States]

Site	White male		Nonwhite male		White female		Nonwhite female	
	Rate	Number	Rate	Number	Rate	Number	Rate	Number
Lip	0.33	4,752	0.06	80	0.03	525	0.04	57
Salivary glands	.44	6,450	.34	497	.22	3,945	.19	317
Nasopharynx	.38	5,759	.58	924	.12	1,988	.15	259
Tongue: Floor of mouth; other parts of mouth and mouth unspecified; oral mesopharynx; pharynx, unspecified	4.21	62,505	4.44	6,575	1.05	18,325	1.30	2,139
Esophagus	4.10	60,819	9.44	13,875	1.03	18,214	2.17	3,575
Stomach	15.22	222,524	24.03	33,606	7.70	137,254	10.69	16,725
Large intestine, except rectum	16.54	241,910	12.07	16,758	16.25	287,645	12.69	19,876
Rectum	7.65	112,232	5,68	7,967	4.82	85,170	4.46	7,110
Biliary passages and liver (stated to be primary site)	5.16	76,070	6.91	10,021	5.34	94,229	4.59	7,261
Pancreas	9.63	142,333	10.17	14,416	5.83	102,899	6.17	9,650
Nose, nasal cavities, middle ear, and accessory sinuses	.43	6,299	.60	886	.23	4,055	.25	403
Larynx	2.54	37,954	2.67	3,898	.24	4,141	.37	607
Trachea, and bronchus and lung specified as primary; and lung and bronchus, unspecified as to whether primary or secondary	37.98	571,226	36.67	53,910	6.29	108,326	6.27	10,222
Breast	.28	4,131	.37	527	25.51	436,618	22.10	36,926
Cervix uteri	NA	NA	NA	NA	7.79	131,240	18.92	32,329
Corpus uteri; other parts of uterus including chorionepithelioma; and uterus, unspecified	NA	NA	NA	NA	6.13	106,455	11.30	18,267
Ovary, fallopian tube and broad ligament	NA	NA	NA	NA	8.57	145,957	6.37	10,696
Prostate	17.84	252,763	27.39	35,397	NA	NA	NA	NA
Testis	.83	12,918	.30	504	NA	NA	NA	NA
Kidney	3.86	57,780	2.67	4,072	1.99	34,204	1.42	2,429
Bladder and other urinary organs	6.78	98,304	5.05	7,001	2.39	43,095	3.05	4,758
Melanoma of skin	1.55	23,417	.39	564	1.11	18,865	.30	492
Other skin	1.51	21,722	.86	1,246	.71	12,937	.62	997
Eye	.23	3,453	.11	200	.19	3,291	.10	196
Brain and other parts of nervous system	4.42	67,751	2.34	4,154	2.91	47,192	1.54	3,022
Thyroid gland	.43	6,436	.36	523	.69	12,032	.70	1,121
Other endocrine glands	.31	4,765	.23	388	.20	3,191	.15	275
Bone (including jaw bone)	1.35	20,368	1.23	1,984	.85	14,403	.88	1,537
Connective tissue	.65	9,775	.59	948	.48	8,009	.50	884
Hodgkin's disease	2.29	35,279	1.65	2,762	1.32	22,340	.78	1,439
Lymphosarcoma and reticulosarcoma; other forms of lymphoma (reticulosis); and mycosis fungoides	4.89	73,475	3.38	5,277	3.25	55,658	1.91	3,283
Multiple myeloma (plasmocytoma)	1.76	26,267	2.70	3,873	1.24	21,460	1.83	2,942
Leukemia and aleukemia	8.81	130,703	5.77	9,327	5.74	95,929	3.88	6,983
All ICD's not previously listed	12.64	186,259	17.19	24,432	9.89	173,690	13.51	21,784
All malignant neoplasms	174.04	2,586,399	186.24	226,592	130.11	2,253,282	139.20	228,561

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[1] Age-adjusted: a method used to make valid statistical comparisons by assuming the same age distribution among different groups being compared.

3-YR SURVIVAL RATE BY CALENDAR PERIOD

[In percent]

Site	1940–49	1950–59	1960–64	1965–69
Esophagus	2	6	6	5
Stomach	12	15	15	15
Colon	36	49	50	50
Rectum	35	47	47	49
Liver	4	2	4	6
Pancreas	2	2	2	2
Lung and bronchus	6	10	11	11
Larynx	47	60	61	67
Breast	63	71	73	72
Cervix uteri	53	64	64	63
Corpus uteri	66	74	75	76
Ovary	30	33	38	35
Prostate	49	59	64	66
Kidney	31	38	44	44
Bladder	48	58	60	62
Tongue	34	41	38	41
Pharynx	25	29	31	32
Melonoma of skin	49	63	69	74
Brain	28	28	33	37
Thyroid gland	67	81	85	86
Lymphoma:				
Reticular cell sarcoma	22	21	20	22
Lymphosarcoma	33	37	41	40
Hodgkin's disease	35	44	53	61
Multiple myeloma	10	13	19	27
Leukemia:				
Acute lymphocytic	0	2	6	15
Acute myelocytic	3	1	1	2
Chronic lymphocytic	33	49	50	53
Chronic myelocytic	16	23	24	26

PREVENTION, TREATMENT OR CURE OF CANCER

Mr. Flood. Has anything happened in the past year to indicate that we have acquired any ability to prevent, to treat, or to cure cancer?

Dr. Rauscher. In terms of treatment the most dramatic advances in the past year have been an increase in our ability to diagnose children with acute lymphocytic leukemia very early and treat them well. Right now something like 50 percent of children diagnosed early and treated aggressively are alive and without symptoms 5 years after treatment. It takes a while as you understand to measure this, but we are measuring it now.

Breast cancer is another major killer of women at high risk age. It seems to be coming under control far better than in the past. This is because of treatment with a combination of surgery together with the use of four or five drugs. The data begin to look awfully good on this.

Mr. Flood. At treatment?

Dr. Rauscher. That is right.

PREVENTION

Mr. Flood. What about prevention?

Dr. Rauscher. In terms of prevention we have identified something like 30 different industrial chemicals known to cause cancer not only in animals but in man. In the past year we have identified vinyl chloride and possibly polyvinyl chloride as substances known to cause cancer.

Recognizing this we have worked with NIOSH and other Government Agencies to begin to protect these workers or to modify the product or do away with the product and use something else.

These are some examples of progress in prevention.

Mr. MICHEL. At this point, Mr. Chairman, we can have the 30 known industrial chemicals identified for the record?

Mr. FLOOD. Without objection we will do that.

[The information follows:]

LIST OF CHEMICALS THAT CAUSE CANCER IN MAN

Individual Compounds:

1. Beta-naphthylamine
2. Benzidine
3. 4-aminobiphenyl
4. 4-nitrobiphenyl
5. Chlornaphazine (bis-2-chloroethyl-2-naphthylamine)
6. Mustard gas (bis-chloroethyl sulphide)
7. Nickel carbonyl
8. Diethylstilbesterol
9. Bis(chloromethyl)ether

Compound Classes:

10. Asbestos
11. Arsenicals
12. Chromates
13. Estrogenic compounds

Manufacturing Exposures:

14. Auramine
15. Magenta
16. Isopropyl oil

Mixtures:

17. Tobacco
18. Tobacco smoke
19. Soots
20. Tars
21. Pitches
22. Asphalts
23. Cutting oils
24. Shale oils
25. Creosote oils
26. High boiling petroleum oils
27. Betel nut (chewing)
28. Various combustion products

Carcinogenicity due to radiation:

29. Radium
30. Thorotrast
31. Uranium ores (radon and radon daughters)
32. Other radioactive materials

CURE FOR CANCER

Mr. FLOOD. Tell us something about cure.

Dr. RAUSCHER. There are about 12 different cancers of the more than 100 diseases that we call cancer that are amenable to cure by treatment with drugs now. Acute lymphocytic leukemia is one. Hodgkin's disease used to be a scourge where we had very, very few survivors. When patients with Hodgkin's disease in early stages are treated aggressively, about 85 percent survive without symptoms for 5 years, and we think many are cured. The secret again is to hit them early and aggressively with the best combination of treatments.

Breast cancer is being cured to an increasing extent with surgery and aggressive radiotherapy, together with chemotherapy. These are not simply longtime survivals, but cures we are talking about.

Mr. Flood. You mentioned about a dozen. For the record will you list all of them?

Dr. Rauscher. Yes.

[The information follows:]

List of Cancers Most Amenable To Cure

Present evidence shows that in 11 types of such cancer, drugs are the critical factor in bringing about normal life expectancy in the percentage of patients shown in table I. In some instances the drugs are used alone, in others in conjunction with surgery or X-irradiation. Virtually all solid tumors are curable in a certain percentage of patients by surgery (or sometimes by X-irradiation) if the tumor is diagnosed before it has spread to distant organs as shown in table II. The failures of surgery (or irradiation) are due to spread beyond the local site. The interesting improvement wrought by chemotherapy is the proof that drugs can cure cancer, after distant spread (metastasis).

TABLE I.—CURE RATES IN 11 TUMORS

	Percent cured prior to addition of chemotherapy	Estimated present percent cured	Time of onset	Approximate number of new cases in U.S. annually
Wilms'	50	90	Infancy	500
Choriocarcinoma	20	80	Young adult	300
Ewing's sarcoma	10	70	Childhood	300
Burkitt's lymphoma	5	70	do	100
Retinoblastoma	20	55	do	200
Acute lymphocytic leukemia	0	50	do	2,500
Mycosis fungoides	5	50	Adult	1,000
Rhabdomyosarcoma	10	50	Childhood	300
Advanced Hodgkin's	5	40	Young adult	5,000
Histiocytic lymphoma	0	25	do	1,000
Metastatic embry. testicular	0	10	do	500

TABLE II.—PERCENTAGE OF PATIENTS CURED

Site	Estimated new cases, in thousands	Percent cured
All sites [1]	656.0	46
Genital organs	125.8	67
Head and neck	23.7	67
Breast	89.7	64
Urinary organs	42.9	62
Digestive organs	166.9	40
Respiratory	95.2	15
All others	26.0	16

[1] Carcinoma-in-situ of the uterine cervix and superficial skin cancers not included in totals.

Mr. Flood. In other words, that phrase down through the years that cancer is incurable is not so as a fact?

Dr. Rauscher. That is not so.

LUNG CANCER

Mr. Flood. What about lung cancer? With all of these things we are doing about lung cancer prevention is the incidence of lung cancer still on the increase?

Dr. Rauscher. In the last 2 or 3 years the slope of the incidence has still been increasing. There is now evidence, beginning about a year and a half ago, that the slope may be plateauing.

Mr. Flood. Is this because we are getting more knowledgeable on operations in this connection or more publicity? Is that producing the statistics or is it something else actually doing it?

Dr. RAUSCHER. I think what is happening is that fewer younger children are beginning to smoke, and we are using cigarette products now of lower tar content.

Mr. FLOOD. I was going to ask you about that.

Dr. RAUSCHER. It is still not good enough.

SMOKING AS A CAUSE OF LUNG CANCER

Mr. FLOOD. Do you believe that smoking is still the chief cause of lung cancer?

Dr. RAUSCHER. There can be no question about it. The conservative estimate is it causes 80 to 85 percent of lung cancer.

Mr. FLOOD. The answer is "Yes"?

Dr. RAUSCHER. The answer is "Yes."

Mr. FLOOD. Would you say the Government's effort to discourage cigarette smoking has been pretty much of a flop?

Dr. RAUSCHER. No, I think there has been a significant——

Mr. FLOOD. I think failure is a better word.

Dr. RAUSCHER. It is a failure in that many people continue to smoke and others take up the habit. On the other hand there are quite a few younger children, where we are making the greatest impact, that do not begin smoking. There is some evidence that adults are switching at least to less hazardous patterns of cigarette consumption. None are without hazards. There can be some success.

SCREENING TEST FOR LUNG CANCER

Mr. FLOOD. Can we look forward for some kind of a breakthrough or some kind of inexpensive screening test for the early detection of lung cancer?

Dr. RAUSCHER. I think so. We have three projects now. They were begun about 2 years ago. One in which by using a fiberoptic device actually inserted into the lungs you can not only see the lesions, the cancer, but you can actually take a piece of it, remove it, and determine whether it is benign or malignant. In some cases small lesions have been detected up to 5 years before the spot shows up on regular X-ray. This is difficult, it takes a lot of sophistication. Your suggestion is much better, of course, something simple and inexpensive. What we are hoping to do is be able to examine in men above the age of 45 who are consistent smokers and using a Pap kind of test to determine whether the cells in their sputum are cancerous. If they are definitive treatment is indicated.

Mr. FLOOD. You said there might be two others you were going to talk about.

Dr. RAUSCHER. Two other forms of cancer?

Mr. FLOOD. You were describing the process.

Dr. RAUSCHER. There are three institutes that are conducting lung cancer detection studies at the present time, and they are Johns Hopkins, Mayo Clinic, and Memorial Sloan-Kettering in New York. There are enzymatic changes that may occur in blood streams of people who are heavy smokers. We hope we will be able to detect and measure the enzymes in blood serum very simply and inexpensively to find out whether the risk is good.

TREATMENT OF LUNG CANCER

Mr. FLOOD. That is detection.

What about the treatment of lung cancer? Are we improving the survival rate?

Dr. RAUSCHER. We are improving the survival rate in a particular form of lung cancer called oat cell carcinoma. It is one of the rarest forms but one of the most malignant. It kills very quickly. Here the successful treatment rate has more than tripled in the past few years.

Mr. FLOOD. What do you mean by quickly?

Dr. RAUSCHER. Less than 6 months from diagnosis, whereas some patients with other forms of lung cancer may survive a year or more.

Mr. FLOOD. Six months from diagnosis?

Dr. RAUSCHER. That is right.

KINDS OF CANCERS WITH GENETIC PREDISPOSITIONS

Mr. FLOOD. Last year you may recall we were talking about the possibility of there being a genetic predisposition to certain types and kinds of cancer. You got all wrapped up in that. Have you learned more about it since last year?

Dr. RAUSCHER. There are a number of diseases, and we can provide these for the record if you like, that do in fact predispose to certain kinds of cancer. This is especially true of children's cancer.

[The information follows:]

KINDS OF CANCERS WITH GENETIC PREDISPOSITION

Only a small portion of cancer is inherited and it is often difficult to distinguish inherited from environmental influences.

Hereditary cancers occur in some offspring of parents with a defective dominant gene. That is, approximately half of the children of an affected person may have the cancer although it may not manifest itself this frequently. The following cancers are known to have genetic predisposition.

HEREDITARY NEOPLASMS AND DESCRIPTION

Retinoblastoma—A cancer of the eye occurring in young children.

Nevoid basal cell carcinoma syndrome—Cancers occurring in the basal layer of the skin.

Trichoepithelioma—Benign skin tumors.

Multiple endocrine adenomatosis—Familial tumors occurring in the pituitary and parathyroid glands and in certain pancreatic cells.

Pheochromocytoma and medullary thyroid carcinoma—Cancers of the adrenal and thyroid glands.

Chemodectomas—A tumor which sometimes develops in the carotid artery or other areas.

Polyposis coli—Numerous benign tumors of the colon and rectum.

Gardner's syndrome—Multiple polyps occurring with a variety of other growths.

Tylosis with esophageal carcinoma—Rare skin changes of the palms and soles in childhood followed by cancer of the esophagus in middle life.

Other cancers occur as a complication of inherited precancerous lesions that are clinically recognizable. These precancerous states are:

1. Haartomatous syndromes.
   Neurofibromatosis.
   Tuberous sclerosis.
   von Hippel-Lindeau syndrome.
   Multiple exostoses.
   Peutz-Jeghers syndrome.
2. Genodermatoses.
   Xeroderma pimmentosum.
   Albinism.
   Werner's syndrome.
   Epidermodysplasia verruciformis.
   Polydysplastic epidermolysis bullosa.
   Dyskeratosis congenita.
3. Chromosome breakage disorders.
   Bloom's syndrome.
   Fanconi's syndrome.
4. Immune deficiency syndromes.
   Ataxia-telangiectasia.
   Wiskott-Aldrich syndrome.
   Late-onset immunologic deficiency.
   X-linked agammaglobulinemia.

Mr. FLOOD. You stirred up interest about it. Did you quit on it?

Dr. RAUSCHER. We are trying to identify children that do have these predispositions. There is a multiplicity of patients with breast cancer as an example, in certain families. This seems to have a genetic familial kind of indicator. We are now trying to identify women with this kind of cancer and instead of getting them to come in once every 2 years for a mammograph or palpation of the breast we can get the high risk individuals to come in two or three times a year in hopes of maximizing the chances for early diagnosis. We have a large program.

MAMMOGRAPHY

Mr. FLOOD. In your budget justifications you actually state that the value of mammography in breast cancer has improved.

Dr. RAUSCHER. That is correct.

Mr. FLOOD. It has been proven. Are you going to do something else? You have proven this now. What are you doing to make it more readily available so that taxpayers can avail themselves of the service? We encounter so many with your long-haired types—OK you do something and there it is, and then you say we found it out and put it away and forget about it. "We discovered that. We can't waste time on that any longer. That is great. Now we must spend all of our time on something we don't know about." What about the fellow up the street?

Dr. RAUSCHER. This is one of the most active components of the cancer control program, and this, again to your point before, is something that was started this past year. We now have 27 new breast cancer detection clinics in cooperation with the American Cancer Society—cofunded with them. These are distributed all over the country; 300,000 women, at no cost to themselves, will be screened for the first time so we can demonstrate to physicians all over the country that this can be done. We are already finding cancer. It is a very young program but we intend to demonstrate once and for all to physicians throughout the country just what can be done with the early diagnosis of cancer which will lead to very high cure rates in women with these cancers. The program costs about $6.5 million at the present time. It is a very active program.

DETECTION OF CANCER OF THE COLON

Mr. **Flood.** We also understand a group of scientists at the Harvard Medical School developed a simple blood test for the early detection of cancer of the colon. Is that being used on a large scale?

Dr. **Rauscher.** It is being used now on a large enough scale to confirm what the people at Harvard have done. There are two things that are being done. They are looking for blood in feces in people with high risk of the cancer.

Mr. **Flood.** This is a simple blood test.

Dr. **Rauscher.** The blood test has to detect the carcinoembryonic antigen, CEA. When present at a relatively high quantity in blood serum these people may have colon cancer, other forms of cancer or sometimes other noncancerous diseases. It is not specific yet.

BUDGET ESTIMATE

Mr. **Flood.** We want to be sure about some of these figures. This is an appropriation hearing. A total of $588.4 million is available for the National Cancer Institute in fiscal 1974. Is that right?

Dr. **Rauscher.** That is correct.

Mr. **Flood.** You are asking for an appropriation of $600 million for 1975. That is an increase of $11.6 million over the funds available for 1974.

Dr. **Rauscher.** Yes.

COMPARISON OF PROGRAM LEVEL FOR 1973, 1974, 1975

Mr. **Flood.** However, we understand that some of that 1974 money is being used to fund grants and to fund contracts for more than 1 year. Do you have any figures there which would show us what you would consider a valid comparison of program level for fiscal years 1973, 1974, and 1975? That we want to see.

Dr. **Rauscher.** Yes, Mr. Chairman. We will submit that for the record.

[The information follows:]

OBLIGATIONS BY BUDGET ACTIVITY SHOWING "TRUE" PROGRAM LEVELS IN 1974–75

[Amounts in thousands]

Budget program	1973		1974		1975	
	Positions	Amount	Positions	Amount	Positions	Amount
Research:						
Cause and prevention research	622	$115, 277	638	$144, 307	647	$153, 215
Detection and diagnosis research	134	26, 973	161	38, 826	168	42, 162
Treatment research	621	144, 568	647	192, 333	653	205, 197
Cancer biology	309	63, 781	317	84, 529	321	90, 231
Resource development:						
Cancer centers support	8	15, 840	12	19, 578	14	23, 484
Research manpower development	4	14, 132	8	24, 010	8	22, 530
Construction	9	39, 151	11	45, 340	11	22, 317
Cancer control	23	5, 512	44	34, 599	51	45, 814
Total obligations	1, 730	425, 234	1, 838	583, 522	1, 873	604, 950

RESTORED 1973 FUNDS

Mr. **Flood**. In your 1974 budget column you include obligations there of $58,859,000 of the funds appropriated in 1973. For the record we want a breakdown of this amount and a brief description of how those funds are being used.

Dr. **Rauscher**. All right.

[The information follows:]

DISTRIBUTION OF 1973 IMPOUNDED FUNDS

[Amounts in thousands]

Budget mechanism	Number of awards	Amount
Research grants	244	$18,394
Cause and prevention research	(35)	(2,650)
Detection and diagnosis research	(6)	(461)
Treatment research	(108)	(8,122)
Cancer biology	(95)	(7,161)
Fellowships (resource development)	110	1,181
Training grants (resource development)	14	4,299
Research and development contracts		19,659
Cause and prevention research		(9,729)
Detection and diagnosis research		(1,534)
Treatment research		(7,606)
Cancer biology		(790)
Construction (resource development)		14,550
Total obligations	368	$58,083

MULTIYEAR AWARDS

Mr. **Flood**. How much will be obligated in fiscal year 1974 for this—I think the term now is—multiple year funding of grants and contracts? What we want is a breakdown there for the record showing how much is being obligated for use in the subsequent years.

Dr. **Rauscher**. Yes, sir.

Mr. **Flood**. That is the catch in this thing.

[The information follows:]

MULTIYEAR FUNDING FROM 1974 APPROPRIATION

[Amounts in thousands]

Budget mechanism	Number of awards	Total amount	Amount affecting 1975 funding
Research grants	80	$9,003,000	$4,950,000
Cause and prevention research	(25)	(2,827,000)	(1,553,000)
Detection and diagnosis research	(7)	(756,000)	(418,000)
Treatment research	(33)	(3,763,000)	(2,069,000)
Cancer biology	(15)	(1,657,000)	(910,000)
Fellowships			
Training grants			
Research and development contracts			

Mr. **Flood**. The table you have on page 23 needs a little adjustment. We want you to include the 1973 appropriations obligated in 1974 and the true program level where these multiple year fundings are involved in that report.

Dr. **Rauscher**. Yes, sir.

[The information follows:]

National Cancer Institute

Obligations by Budget Mechanism
Showing "True" Program Levels
in 1974 - 1975
(Amounts in Thousands)

Budget Mechanism	1972 No.	1972 Amount	1973 No.	1973 Amount	1974 Estimate No.	1974 Estimate Amount	1975 Estimate No.	1975 Estimate Amount
Grants								
Regular								
Non-competing	694	$36,417	1,013	$54,688	1,030	$64,532	1,240	79,462
Competing	588	32,892	501	31,515	689	45,671	533	40,628
Renewal	(204)	(13,346)	(129)	(10,365)	(243)	(16,852)	(208)	(16,837)
New	(384)	(17,122)	(372)	(18,085)	(446)	(24,617)	(325)	(20,265)
Supplemental	---	(2,424)	---	(3,065)	---	(4,202)	---	(3,526)
Subtotal	1,282	69,309	1,514	86,203	1,719	110,203	1,773	120,090
Special								
Cancer research centers	99	50,203	127	65,100	142	87,795	141	100,834
Task Forces	6	638	51	3,950	128	10,503	114	11,500
Research Career Program	85	2,026	75	1,818	91	2,099	86	2,000
Scientific Evaluation	---	---	---	279	---	279	---	326
Clinical Education Program	---	---	---	---	---	---	67	4,000
Radiation Development	---	---	3	2,410	3	3,360	3	4,250
Subtotal	190	52,867	256	73,557	364	104,036	411	122,910
Total Grants	1,472	122,176	1,770	159,760	2,083	214,239	2,184	243,000
Fellowships								
Non-competing	15	136	30	314	42	454	394	5,516
Competing	182	1,785	61	674	500	6,631	536	6,550
Renewal	(19)	(193)	(14)	(136)	---	---	---	---
New	(163)	(1,592)	(47)	(538)	(500)	(6,631)	(536)	(6,550)
Supplemental	---	---	---	---	---	---	---	---
Subtotal	197	1,921	91	988	542	7,085	930	12,066
Training Grants								
Non-competing	120	10,894	146	10,100	169	12,259	107	6,097
Competing	81	5,580	47	2,800	14	4,299	---	---
Renewal	(62)	(4,335)	(47)	(2,713)	---	---	---	---
New	(19)	(1,084)	---	---	(14)	(930)	---	---
Supplemental	---	(161)	---	(87)	---	(3,369)	---	---
Subtotal	201	16,474	193	12,900	183	16,558	107	6,097
Intramural Laboratory and Clinical Research	---	12,388	---	13,953	---	16,265	---	17,127
Research and Development Contracts	---	122,049	---	136,161	---	180,369	---	180,494
Collaborative Research & Support	---	24,766	---	31,200	---	34,399	---	37,353
Research Management & Program Services	---	21,807	---	26,246	---	35,519	---	41,715
Construction	---	51,003	---	38,804	---	45,033	---	22,000
Cancer Control	---	---	---	5,222	---	34,055	---	45,098
TOTAL	---	$372,584	---	$425,234	---	$583,522	---	$604,950

REGULAR RESEARCH GRANT PROGRAM

Mr. **Flood**. Will this 1975 budget maintain the regular research grant program at the 1974 level?

Dr. **Rauscher**. There will be increases of $18 million in 1975.

Mr. **Flood**. What?

Dr. **Rauscher**. We are cutting down on some of our construction in order to put more money into the operational aspects of regular research grants. So the total increase for research grants in 1975 will be of the order of $18 million.

Mr. **Flood**. I understand that, but the question was will the 1975 budget which you are here on maintain the regular research grant program at the 1974 level?

Dr. **Rauscher**. It will maintain that level in terms of funding. In terms of percentage of payable projects it will decrease.

Mr. **Flood**. What is that?

Dr. **Rauscher**. We are getting more and more people applying for cancer funds, so the percentage of approved new projects that we will be able to pay will decrease from this fiscal year.

NEW RESEARCH GRANTS

Mr. **Flood**. You have a table on page 23. Take a look at it. It indicates there will be less money for new research grants in 1975, but you are going to fund a larger number of grants. How are you going to make more grants with less money? That is a good trick. How do you do that?

Dr. **Rauscher**. The budget level there is a comparison of $530 million to $600 million, not $589 million which is the obligational authority this year. So with the released funds these figures will increase substantially.

Mr. **Flood**. This is on page 23. Grants, regular, down to new. The number is 279, the amount is $21,474,000. In 1975 you say the number is 325 and the amount is $20.265,000. That is as plain as the nose on your face. What about that? If you were sitting here and I was down there, would you ask me about that?

Dr. **Rauscher**. You are saying the number is increasing from 279 to 325.

Mr. **Flood**. You have more grants and less money, yes. The numbers are from 279 in 1974 to 325 in 1975.

Dr. **Rauscher**. That is right.

Mr. **Flood**. And less money. How do you do that?

Mr. **Browning**. That is because we are putting more money in the noncompeting grants.

Mr. **Flood**. I would like to find out the answer to that. I could use it.

Mr. **Browning**. The total money for regular grants is the same for the 2 years.

Mr. **Flood**. What?

Mr. **Browning**. Excuse me. On page 23 the 1974 column is based on $530 million rather than the $588 million in which we include the impounded funds, the $58 million from 1973.

Mr. **Flood**. I know what you mean.

Mr. **Browning**. The reason for the reduction in the new grants is because we need $10 million more for noncompeting grants on the first line. It goes up $10 million.

Mr. **Flood**. I know that. This is all very fine but let's go back. How do you get more grants with less money? That is where I started.

Mr. **Miller**. Can I make a guess?

Mr. **Flood**. Yes.

Mr. **Miller**. The amount per grant is less. They are funding less costly grants and there are going to be more of them I guess.

Mr. **Browning**. It is the estimated cost of grants. The average cost of the grant changes.

Mr. **Flood**. That was an educated guess. But isn't it a fact that the cost per grant is going up as everything else is?

Mr. **Miller**. It is a possibility that they may be funding fewer million dollar grants and more $300,000 grants.

Dr. **Rauscher**. That is true.

Mr. **Flood**. That is the best you can do?

Dr. **Rauscher**. We are also funding more and more younger investigators.

CANCER CENTERS

Mr. **Flood**. I can't understand why you are surprised I asked you that one.

On the cancer centers, in the budget justifications you state that the cancer centers program is evolving into "A geographical balanced combination of specialized and comprehensive cancer centers."

You gave us a list there of the 15 comprehensive centers. We also want the 49 specialized cancer centers.

Dr. **Rauscher**. Yes, sir.

[The information follows:]

LIST OF SPECIALIZED CANCER CENTERS

1. Columbia University College of Physicians and Surgeons, New York.
2. State University of New York, New York.
3. Mallory Institute, Massachusetts.
4. University of California, California.
5. Tulane University School of Medicine, Louisiana.
6. Stanford University, California.
7. University of Maryland, Maryland.
8. Yale University, Connecticut.
9. Institute for Cancer Research, Pennsylvania.
10. Michigan Cancer Foundation, Michigan.
11. Montefiore, Hospital and Medical Center, New York.
12. Baylor College of Medicine, Texas.
13. Massachusetts General Hospital, Massachusetts.
14. Cancer Research Center, Missouri.
15. St. Jude Research Hospital, Tennessee.
16. University of Minnesota, Minnesota.
17. Allegheny General Hospital, Pennsylvania.
18. Wistar Institute, Pennsylvania.
19. University of Rochester, New York.
20. Institute for Medical Research, New Jersey.
21. Howard University, District of Columbia.
22. Temple University School of Medicine (Fellowships Institute), Pennsylvania.
23. Jefferson Medical College, Pennsylvania.
24. M.I.T., Massachusetts.
25. Tufts-New England Medical Center, Massachusetts.

26. Bowman Gray School of Medicine, North Carolina.
27. Children's Hospital of Denver, Colorado.
28. American Health Foundation, New York.
29. Worcester Foundation, Massachusetts.
30. Washington University, Missouri.
31. Cold Spring Harbor Laboratory, New York.
32. Albert Einstein College of Medicine, New York.
33. New York University Medical Center, New York.
34. University of Colorado Medical Center, Colorado.
35. Children's Hospital Medical Center, Massachusetts.
36. Indiana University Foundation, Indiana.
37. Medical College of Virginia, Virginia.
38. Roger Williams General Hospital, Rhode Island.
39. University of New Mexico, New Mexico.
40. University of Texas Medical Branch, Texas.
41. University of Pennsylvania, Pennsylvania.
42. Hospital for Joint Diseases, New York.
43. Salk Institute for Biological Studies, California.
44. Cornell University, New York.
45. Children's Hospital of Philadelphia, Pennsylvania.
46. University of Chicago, Illinois.
47. Georgetown University, District of Columbia.
48. Harvard Medical School, Massachusetts.
49. University of Connecticut, Connecticut.
50. Wayne State University, Michigan.
51. University of Kansas, Kansas.
52. Mountain States Tumor Institute, Idaho.
53. University of California, Los Angeles, California.
54. University of California, San Francisco, California.

Included in this list are those centers which will attain comprehensive status during fiscal year 1974, leaving a total of 49 specialized cancer centers.

COMPREHENSIVE AND SPECIALIZED CENTERS

Mr. Flood. Can you explain to us how these Comprehensive Centers and the Specialized Centers work together? Better tell us about that.

Dr. Rauscher. Within a given geographic area there may be four or five different Cancer Centers, as in New York City or Philadelphia as an example. They may have expertise in radiotherapy or chemotherapy, or may be almost totally research. These together, informationwise, work with any Comprehensive Center that happens to be in that area. We are trying to tie these together in a communications network all over the country.

Mr. Flood. Communications network? You are going to set up your own communications network between the Centers?

Dr. Rauscher. To the extent that the Comprehensive and Specialized Centers report information on an annual basis to the National Cancer Institute. Then it is made available to other Centers within the entire country.

Mr. Flood. What is the communications? You are not going to have TV sets in New York and TV sets in San Franciso.

Dr. Rauscher. It is a publication kind of communication, a sharing of patient data on the best methods of treating a cancer patient.

Mr. Flood. How many of these Comprehensive Centers do you intend to set up under the cancer program?

Dr. Rauscher. We now have 12 as you know. There are 4 to 6 more that will be recognized before the end of this fiscal year. The best judgment estimate we have right now is that in order to bring a major share of the population within 60 to 120 miles of a Center we may have to go to something like 30 to 32 Comprehensive Centers in the country.

Mr. Flood. How many of the Specialized Centers do you intend to set up?

Dr. Rauscher. We have no target for Specialized Centers. As newer institutions become established and apply for Specialized Cancer status, we will have our regular peer review system review their proposals and fund them accordingly.

CREATION OF NEW CANCER CENTERS

Mr. Flood. When would you like to have those additional Centers in operation?

Dr. Rauscher. I would like to have them within the next 2 or 3 fiscal years. I think it is going to take a little longer than that.

Mr. Flood. That is what you would like. When will they actually be in operation?

Dr. Rauscher. If we are talking about 30 to 32 Centers, I would estimate right now it would take another 5 to 8 to 10 years.

Mr. Flood. Five to 8 to 10?

Dr. Rauscher. Remember, we are going to continue to support our Specialized Centers. Some of these will eventually attain comprehensive status. Some will choose not to go that way, and I think this is wise.

COLLABORATIVE EFFORTS WITH OTHER AGENCIES

Mr. Flood. In your justification again you mention a collaborative effort with several Federal agencies. The minute you start collaborating with Federal agencies that causes some concern.

We have been through hearings on this. How do you work with the National Institute for Occupational Health and Safety in identifying potential carcinogenic chemicals in the workplace over there?

Dr. Rauscher. Two ways, Mr. Chairman. When we find that there is a higher incidence than expected

Mr. Flood. This is red hot.

Dr. Rauscher. It certainly is. When we find there is a higher incidence than expected of certain kinds of tumors—a good example here is those unusual liver cancers seemingly induced in workers exposed to vinyl chloride—we bring this to the attention of people in NIOSH and help them set up a surveillance system to determine just what other workers have been exposed, the duration of exposure, and the expected case rate.

We provide virtually weekly consultation in terms of biometric analysis to the people in NIOSH in evaluating patients that have developed cancer. They in turn seek information from us all the time and we from them.

COLLABORATIVE EFFORTS WITH ENVIRONMENTAL PROGRAMS

Mr. Flood. Of course you have been reading about this. By the way I was raised in St. Augustine, Fla., and I have never seen that town get so much attention since Ponce de Leon's time at the annual meeting down there.

I have before me now a story from the New York Times, March 23, 1974, published in the green sheet, the HEW publication "The Discovery of Rare Cancers Causes Concern About Environment." I think we ought to put this in the record because you may want to comment on that specific information. We have a dozen of these things but this deals specifically with the question of very much concern to this committee that we have been going through with OSHA.

We held hearings on the Department of Labor and finished the hearings, and all the members examined all these people at great length about this one thing. What about that? I can't think of anything more important in the OSHA show than this question.

Dr. RAUSCHER. I certainly agree.

[The information follows:]

RARE CANCERS IN THE ENVIRONMENT

Cancer prevention through the identification of environmental carcinogens and reduction of exposure to these carcinogens is a major goal of the national cancer program, since available evidence suggests that environmental agents and social practices are responsible for an overwhelming percentage of cancer cases in this country. Vinyl chloride is a chemical that forms a basis for much of the modern plastics industry and is used in numerous consumer aerosol products, such as cosmetics, pesticides, and household items. The evidence now being accumulated suggesting a link between vinyl chloride and cancer of the liver has, therefore, sparked a high priority cooperative effort between the National Institute for Occupational Safety and Health, the Labor Department's Occupational Safety and Health Administration, private industry, and the National Cancer Institute to determine the exact extent of risk from vinyl chloride and what precautions will be needed to protect industrial workers and possibly the consumer as well. The Institute's role in this cooperative effort consists at this time of several research efforts by various branches of the Institute.

For instance, scientists in the Division of Cancer Cause and Prevention of the National Cancer Institute are lending their expertise and providing advice to the other agencies involved in this cooperative effort at a series of meetings that have been and will be held by those agencies on the subject of vinyl chloride and angiosarcoma of the liver.

Also, the Institute's Biometry Branch is studying the overall incidence and mortality from angiosarcoma of the liver in the total U.S. population and looking at the characteristics of these patients in an attempt to identify occupational factors responsible for this disease. Moreover, by determining the normal incidence of this disease in the general population, we will be able to provide a base on which to gage the true proportions of the problem among industrial workers.

The Laboratory of Pathology of the National Cancer Institute has received slides from Prof. Cesare Maltoni, director of the Istituto di Oncologia in Bologna, Italy, who experimentally created liver angiosarcomas in rats inhaling vinyl chloride. This laboratory will be inspecting these slides to confirm Dr. Maltoni's diagnosis.

As the research on vinyl chloride progresses, the Institute will continue to be of any possible assistance to this cooperative effort and will no doubt be undertaking further research activities on vinyl chloride.

[From the New York Times, Mar. 23, 1974]

DISCOVERY OF RARE CANCER SPURS CONCERN ABOUT ENVIRONMENT

(By Jane E. Brody)

ST. AUGUSTINE, FLA., March 22.—The recent discovery of a rare liver cancer among workers exposed to vinyl chloride has enhanced the concern of some scientists about the myriad substances in the general environment that are known or suspected of causing cancer.

This concern was voiced here today at the opening session of the American Cancer Society's annual seminar for science writers by Dr. Irving J. Selikoff and Dr. E. Cuyler Hammond, who are studying the consequences of exposure to vinyl chloride and other occupational agents.

ALTERED ENVIRONMENT

Vinyl chloride exposure has thus far been linked to a dozen cases of angiosarcoma of the liver, an invariably fatal tumor, among workers involved in transforming the chemical into polyvinyl chloride, a basis for much of modern plastics. Vinyl chloride is the formulation for countless consumer products, and millions of Americans are potentially exposed to its effects.

But Dr. Hammond, vice president for epidemiology and statistics of the American Cancer Society, said in an interview, "vinyl chloride is only an example of a much broader problem."

"In the past 40 years, the environment in which we live has been altered to an extraordinary extent," Dr. Hammond and Dr. Selikoff wrote in a background paper. "The air we breathe contains gases and particles that never before entered the human lung. Our food has chemicals designed to improve its taste, freshness, appearance—but which are strange to our intestines, livers, kidneys, blood."

They continued, "We touch, ingest, inhale, absorb an ever-increasing number of synthetic materials and, in other circumstances, agents which may have existed on Earth but were never part of the immediate human environment."

The plaguing question behind these changes, they said, is how many may be responsible for the estimated 655,000 new cases of cancer that will be diagnosed among Americans this year? And how many will cause cancer 20, 30, or 40 years from now? The World Health Organization estimates that some 25 percent of human cancers result from exposure to environment agents.

Since cancer usually does not show up until 20 or more years after initial exposure to a cancer-causing substance, the scientists said that "prevention of cancer in the year 2000 is the order of the day in 1974."

The problem is where and how to begin. "There are perhaps 10,000 new chemicals put into production each year," Dr. Hammond noted. "Should every one of these be tested in animals? Obviously this can't be done thoroughly, and if it were done superficially, you wouldn't find anything."

Instead, Dr. Selikoff, director of environmental sciences laboratory at Mount Sinai Medical School in New York City, suggested that testing be limited to those substances that are relatives of known cancer-causing substances and those to which workers and the general public will be widely exposed.

Dr. Hammond pointed out that animal tests may not tell the whole story. He cited a study of roofing workers to show that one cannot reach hasty conclusions about the risk to man on the basis of animal studies.

Roofers are exposed to very high concentrations of a chemical called benzpyrene, a substance in tobacco smoke and pollutant of air that for decades has been known to readily cause cancer when painted on the skin of laboratory animals. But even when inhaling levels of benzpyrene equivalent to smoking perhaps hundreds of unfiltered cigarettes a day, roofers experience only a slight increase in lung cancer rates, Dr. Hammond reported.

"If benzpyrene were what is causing lung cancer in smokers, these roofers should have experienced a colossal increase in lung cancer," Dr. Hammond said.

The moral of this story, he said, is that "if you take the view that any substance that causes cancer in animals should be banned from human use, we would be getting rid of substances that are relatively innocuous to man."

On the other hand, he added, "the vinyl chloride hazard could have been predicted from animal experiments, and such experiments are the only means we have for getting an early warning of what might happen in man."

Therefore, he also urged that any substance that will be put into wide use should be tested by the Government before people have been exposed to it for many years, and that registries of exposed workers should be established to follow the posible effects of the substance.

"We have to develop methods of testing such that we won't always be faced with an emergency situation, as we now are with vinyl chloride," Dr. Hammond concluded.

Dr. STONE. You do recognize that the National Institute of Environmental Health Sciences is engaged in related, collaborative, complementary efforts?

Mr. FLOOD. That is good, yes.

When I picked up this article, I think I cut you off before you got to the verb someplace. Were you going to say something else?

Dr. RAUSCHER. I was trying to explain how we do collaborate with other Government agencies, OSHA in particular.

CANCER MORTALITY DATA BY U.S. COUNTY

Mr. FLOOD. In the justification again, you state through the field studies cancer mortality in the United States can be shown at a county level. What are you doing about the counties that show up at the top of the list? There they are. What about those?

Dr. RAUSCHER. What we are trying to do in identifying high-risk populations in general, whether they be in a county or in a particular factory, is to then go in with our teams of epidemiologists and chemical carcinogenic people, and try to identify reasons why that might be a high-risk geographic area in which to live. Through these studies we are able to say that something like 20 different chemicals cause cancer in man. The next step obviously is to try to eliminate the identified hazard which is precisely what we are trying to do with vinyl chloride and asbestos.

Mr. FLOOD. Here is one thing I want to go into at some length. It is from the Washington Post article I have in my hand, March 20, 1974. It is an article by Stu Auerbach, and there are a number of serious charges here. I simply can't take the time now to go into this newspaper article as I want to. It is very serious. I am going to insert it. I want you to comment on this. You have probably seen it.

Dr. RAUSCHER. Yes.

Mr. FLOOD. I also have a series of questions I was going to ask you, but in the interest of time will not. Many of these questions will be related to this newspaper article. I want you to look at those, will you?

[The information follows:]

CANCER VIRUS PROGRAM HIT BY SCIENTISTS

Most of the points made in this article were addressed in Dr. Rauscher's earlier testimony before Congressman Flood. However, the following is a brief review of the NCI response to several of the comments made by the Zinder report on the special virus program.

First of all, the Zinder report is essentially a good report. However, it is based to some extent on a dislike and misunderstanding of the contract mechanism and how it has operated within the special virus program. In this instance, the contract mechanism was chosen in order to get the initial program (special virus leukemia program) going more quickly and in order to support research and development investigators in private commercial laboratories, which by definition do not qualify for grant support.

The Zinder committee also suggests that basic research was compromised in order to pursue one area of cancer research which might lead to a scientific breakthrough. NCI does not believe this was the case with the initial special virus program. This program was started not only to exploit existing information through a targeted coordinated effort, but also to generate and expand the base of fundamental information so that additional advances could be made toward the control of cancer in man. Another major goal of the program was to encourage topnotch investigators to enter the field of tumor virology. In 1965 when the program started, there was a scarcity of qualified investigators involved in the difficult and complex field of virus-cancer research; now there are many interested in this area of research.

In summary, it should be reiterated that all modifications of this program as recommended by the Zinder committee and endorsed by the National Cancer Advisory Board will be implemented as soon as possible, and the Institute will continue to consider the studies such as those conducted by the Zinder committee as a model for evaluation of other programs directed by the National Cancer Institute.

[From the Washington Post, Mar. 20, 1974]

CANCER VIRUS PROGRAM HIT BY SCIENTISTS

A blue-ribbon committee of scientists yesterday accused the Government's 10-year-old, $250 million program on cancer-causing viruses of failing to support needed basic research and of having an inbred management replete with conflicts of interest.

As a result, "promising scientists are not being funded today," the panel's chairman, Dr. Norman Zinder of Rockefeller University in New York, told the National Cancer Advisory Board.

The committee was picked by the advisory board, which oversees the Federal war on cancer, to study complaints among scientists that the National Cancer Institute's program to find cancer viruses was not worth the money spent on it.

"It is a truism," Zinder said "that high productivity from a research program so broad in scope is essentially impossible when control is largely in the hands of a few individuals.

"There is an inordinate amount of power in the segment chairmen (NCI officials who grant contracts). It is this power that is responsible for the tensions that exist among contractors in the program and accounts for the apathy to the program in the scientific community."

Zinder's committee charged that NCI scientists in the program often have a conflict of interest in the contracts they award because they do research in labs they approve grants for.

"Those who run it," the committee report said, "are also often the recipients of large amounts of the money they dispense."

"Our own analysis," said Zinder, "is that about 50 percent of the program is supportable at some level."

Committee members—who sat in on meetings between NCI officials and companies seeking contracts—reported that the Government review was poor.

"We are quite sure," the committee reported, "that much more would have been accomplished if equal support had been provided on a competitive basis to many more laboratories with greater capability and experience in particular areas."

The committee did say, however, that scientists supervising the programs include some of the best researchers in the field. The cancer virus program is headed by Dr. John M. Moloney, who discovered a basic virus used in cancer research. Other scientists include Dr. Robert J. Huebner and Dr. George Todaro, who have developed innovative theories on how cancer viruses work.

The committee agreed that the Government should hunt for viruses that cause cancer in humans.

But, it reported, we "reject the concept that this holds sufficient promise for a short-term solution to the cancer problem to justify compromising basic research in this and other areas."

The committee said there was not enough knowledge when the program started in 1964, nor is there enough now "to mount such a narrowly targeted program.

"Basic ignorance of the mechanism involved in the cancer process, even in animals where a viral etiology (cause) is definitely established, is so profound that it is difficult to be certain where to begin, much less organize a focused attack."

The committee recommended that the program be continued, but that it be opened up to more outside scientists who would give projects stricter reviews before approving them.

Dr. Frank J. Rauscher, Director of the National Cancer Institute, called the committee's report "very good," but said that when the program began there were not as many good people in the field as there are now. As a result, he said, people giving the contracts were often doing work under them.

He said that many shortcomings mentioned by the committee are being corrected.

TRAINING GRANTS AND FELLOWSHIPS

Mr. FLOOD. On research manpower, does this budget continue the phase-out of the training grants?

Dr. RAUSCHER. It does, of the classic or traditional training grants.

Mr. **Flood**. Are you expanding fellowships in 1975?

Dr. **Rauscher**. Yes, and the clinical education program. We are awarding funds to medical schools, osteopathic schools, and so forth, to expose new physicians to cancer-related activities.

Mr. **Flood**. Now that you have the release of the 1973 money and the restoration of the 1974 money, of those fellowships and the training grants which were previously phased out do you think there is enough money in this budget to support continuation of these?

Dr. **Rauscher**. There will be enough to honor our moral commitments for previously approved grants——

Mr. **Flood**. To honor what?

Dr. **Rauscher**. Moral commitments to training grants and to fellows.

Mr. **Flood**. What is a moral commitment?

Dr. **Rauscher**. If a person applies——

Mr. **Flood**. It is a commitment, period.

Dr. **Rauscher**. If a person applies for 3 years and is approved and we fund him for the first year, we commit future year funding. We can do that with released funds, yes.

CLINICAL EDUCATION PROGRAM

Mr. **Flood**. Do you propose to initiate a new clinical education program?

Dr. **Rauscher**. Yes.

Mr. **Flood**. Tell us how it will work.

Dr. **Rauscher**. We will provide funds to medical schools, dental schools, schools of osteopathic medicine, and other institutions. We want these people exposed to the newer methods in diagnosing cancer and in treating cancer. We want them to develop other innovative forms of getting the kind of information we have now out to people practicing medicine in the field and, most importantly, to the people just being trained to go out into the field. This will be funded at a level of $4 million in 1975.

CANCER CONTROL

Mr. **Flood**. You are asking for a pretty substantial increase for cancer control activities.

Dr. **Rauscher**. Yes, sir.

Mr. **Flood**. Can you tell us why you need that increase and how you will spend it?

Dr. **Rauscher**. This is the most important new element of the cancer program. It is the program which translates research findings into demonstrating to people what can be done for preventing, diagnosing, and treating cancer. The program had a zero funding base 2 years ago. It went to $5 million in 1973 and $34 million in 1974. It is a minimum we need to take advantage of existing information now for patients and other concerned people.

Mr. **Flood**. We are pretty excited about what you say, but it it true that this activity transmits all this cancer detection, diagnosis, and treatment information to the physicians and to the general public?

Dr. **Rauscher**. This is the program which does that; yes, sir.

Mr. **Flood**. How successful have you been, do you think?

Dr. **Rauscher**. I think we have been remarkably successful already. We have had this authority now for only about 2½ years. Already we have a program that will make it possible for 300,000 women to be screened for breast cancer. We have pap test centers being set up with many States. This is a program with a direct impact on people.

PAP TEST

Mr. **Michel**. Still only 25 percent of the women avail themselves of the pap test?

Dr. **Rauscher**. That is right, but as of a year ago that was the story. Twenty-five percent of women have never had more than two pap tests. Forty percent have had one. This is why we are going into this kind of thing, to get it out to more people at high risk.

Mr. **Michel**. It's been pretty static. It is always about 25 percent.

Mr. **Flood**. That is right.

Mr. **Michel**. What do we do to get it to 50 percent?

Dr. **Rauscher**. That is why we are putting about $5 million into the cancer control program, to really get at that issue.

Mr. **Flood**. Every time I go some place, no matter where it is, receptions, dinners, parties with the medical people, we always wind up with this figure. They are excited about a big deal, but it is always 25 percent.

Dr. **Rauscher**. We will improve that.

Mr. **Flood**. There is something magic about that.

Dr. **Rauscher**. We will improve it significantly with these funds.

LACK OF AUTHORIZING LEGISLATION

Mr. **Flood**. I have the impression there is no legislative authority for the appropriations for the National Cancer Institute for fiscal year 1975. Is that right?

Dr. **Rauscher**. Yes; no specific authorization.

Mr. **Flood**. No legislative authority for the appropriation?

Dr. **Rauscher**. Not yet. It is in committee right now.

Mr. **Flood**. As of this morning?

Dr. **Rauscher**. That is right.

Mr. **Flood**. What is the status of that legislation?

Dr. **Rauscher**. We understand——

Mr. **Flood**. Put it in the record.

Dr. **Rauscher**. We are told the House probably will report out its bill within the next week or 2.

[The information follows:]

Status of Cancer Legislation

At this writing the Senate has approved S. 2893 but the House has not yet voted on H.R. 13053, although it has been approved by the full Committee on Interstate and Foreign Commerce. It is anticipated the House will approve H.R. 13053 in the very near future.

Since there are differences between the Senate and House bills a conference committee will have to consider the two versions and arrive at a single bill. This is expected to be accomplished with a minimum of delay and the resulting single bill should then be approved by both Houses and sent to the President for signature.

Mr. FLOOD. Do you expect any changes in the legislation?

Dr. RAUSCHER. There will be.

Mr. FLOOD. Material ones?

Dr. RAUSCHER. Yes.

Mr. FLOOD. Do you have any authority anyplace else you can find around in the Public Health Service Act under which funds could be appropriated for the National Cancer Institute in 1975?

Dr. RAUSCHER. I am told the answer is yes. Section 301 of the PHS Act does that.

Mr. FLOOD. Let us have that.

[The information requested follows:]

AUTHORITY IN THE PUBLIC HEALTH SERVICE ACT

If legislation now before the Congress to continue the authorities of the National Cancer Act of 1971 (Public Law 92-218) does not become law prior to July 1, 1974, all of the authorities of that act continue with the exception of the authorization levels for the National Cancer Institute and the Cancer Control Program. However, the Cancer Institute could continue to operate its programs through section 301 of the Public Health Service Act; that section which authorized expenditure of funds prior to passage of Public Law 92-218. The one exception to this is the authority for the Cancer Institute to enter into contracts—this authority lapses in 1975 according to section 301(H) of the Public Health Service Act. DHEW will soon submit legislation to extend this contract authorization.

Mr. FLOOD. Is there anything in your budget which would not be covered by that authority?

Dr. RAUSCHER. I don't think so.

LAETRILE

Mr. FLOOD. I have an article from the Washington Star, but this goes back to December 7. It has to do with laetrile. Recently there has been developing a lot of action again on this question of laetrile. Why do you deprive this person of this or that right? They are hopeless and you know the story.

Dr. RAUSCHER. Yes.

Mr. FLOOD. This is a constitutional right. To what degree is it a right? Now that you abandon all hope you say you cannot have it. We must have something more from you and your people right now on this. To begin, I have this article from the Star, one of Judy Randal's articles.

Dr. RAUSCHER. Yes.

Mr. FLOOD. I don't know who wrote the lead. It is a good lead. Go on from there, will you?

Dr. RAUSCHER. I certainly will.

EXPIRATION OF CONTRACT AUTHORITY

Mr. MILLER. If I may make a point to apply to the NIH Institutes which took me by surprise this year. That is, the contracting authority under section 301(h) of the Public Health Service Act runs out. It was an 8-year authority and it runs out at the end of fiscal year 1974. We will request legislation to extend that.

Mr. FLOOD. What about the law?

Mr. MILLER. This applies to all the Institutes.

Mr. **Flood.** Most people cannot understand this question of authorization. People can't understand it. "How is it, Congressman, that you can vote to authorize $5 billion for the following series of projects and then 6 months later appropriate only $2 billion? How do you do that?"

Schoolteachers and professionals do not understand the difference between authorization and appropriation. You and I know, but it is extraordinary the people who cannot put that together.

NEWSPAPER ARTICLES

I have a collection of articles which I have been clipping out. I will go over this with the staff and some of these will be placed in the record and I will ask you to respond.

Dr. **Rauscher.** Very well.

[The information referred to follows:]

War on Cancer Hit as Mythical

This newspaper article accurately reflected the position taken by Dr. Rauscher in his memorandum to the Office of Management and Budget regarding the national cancer program. It should be pointed out that the Office of Management and Budget requests such information on different budget levels each year from virtually all Government agencies. Within any total national budget no individual program can ever do everything that is possible or desirable. Priorities must be established at the national level just as priorities must be established in cancer research. The article was right in pointing out that more funds could be used well. This view, however, is tempered by the concern that such funds not be provided at the expense of other areas of biomedical research nor to the detriment of other important priorities of this Nation.

The total amount appropriated for the National Cancer Institute for fiscal year 1972 was $378,794,000 representing an increase of $148,411,000 over the previous year's appropriation. Because no appropriation bill for the 1973 fiscal year was enacted, the Institute operated under a continuing resolution and was permitted to spend $433 million.

For fiscal year 1974, the current year, the President signed into law an appropriation bill passed by the Congress providing $551 million for the National Cancer Institute. The bill contained a provision which allows a reduction of 5 percent of any appropriation. Within the 1974 appropriation and the release of 1973 appropriated funds for use in 1974, the amount available to the National Cancer Institute for fiscal year 1974 is $588,472,000.

[From the Washington Star-News, Aug. 1, 1973]

War on Cancer Hit as Mythical

Two Democratic Senators have disclosed internal Government memorandums in support of their contention that "the much ballyhooed conquest of cancer program is more a myth than a reality and that research budgets to combat other dread diseases have been gutted on the pretext of maintaining that myth."

The National Institutes of Health memorandums were collected during the preparation of a General Accounting Office report on the Department of Health, Education, and Welfare.

They were released at a news conference yesterday by Senator Mike Mansfield, Democrat, of Montana, the Senate majority leader and Senator Warren G. Magnuson, Democrat, of Washington, chairman of the Senate appropriations subcommittee for Labor and Health, Education, and Welfare.

Two of the memorandums—written last fall by Dr. Robert Q. Marston, who was fired as National Institutes of Health director in January—pointed out that budgetary restrictions on the cancer program were impeding the development of "fundamental new information flowing from basic laboratory work" and that without this information no "major revolution in the prevention and treatment of cancer" could be expected.

Marston also warned at the time of serious imbalances between "politically visible" spending for cancer and heart disease and spending for other kinds of biomedical research—despite previous assurances from the Nixon administration that such imbalances would not occur.

Referring to the Nixon budget for fiscal 1974, as it was taking shape in December, Marston expressed concern for a plan that would increase cancer spending by $208 million, heart and lung disease spending by $28 million and spending for all other diseases combined by only $28 million at a time when inflation was eroding purchasing power.

This meant, he pointed out, that spending for biomedical research in fields other than heart disease and cancer would drop by $111 million in the 2-year period between fiscal years 1972 and 1974.

Other internal Government memorandums uncovered by the General Accounting Office disclosed a number of National Institutes of Health programs which are being particularly adversely affected by fiscal constraints.

For example, although 6,000 Americans die each year from poisoning by anesthetics and an undersupply of qualified personnel, efforts to remedy this situation by the National Institute of General Medical Sciences have been severely curtailed.

And although the National Eye Institute has made substantial progress toward improved methods for treating glaucoma, lack of money to further advance research against the Nation's leading cause of blindness has made further study "impossible."

The Nixon administration proposed cancer budget for the current fiscal year is $500 million—$140 million less than it promised when the Conquest of Cancer Act became law in 1971.

Another memorandum written in November by Dr. Frank J. Rauscher, director of the National Cancer Institute was also released yesterday and spelled out more than 25 "deleterious effects" to be expected as the result of the cut. Among them:

A reduction in the number of chemicals entering the environment—about 5.000 new ones each year—that can be screened for their cancer-causing potential.

Research restrictions on immunotherapy and immunodiagnosis—which together "offer the most immediate" hope for improved detection and treatment of major cancers.

Restrictions on the development and introduction of new cancer drugs.

Slowing of efforts to develop a safer cigarette.

Delay of studies of four newly discovered cancer viruses that are thought to cause cancer in man and consequent delay of methods to prevent infection by them.

Last year President Nixon vetoed congressional appropriations for Health, Education, and Welfare and all its programs have been operating on a continuing resolution.

In an effort to prevent another veto, Magnuson said yesterday that this year's bill will be delayed until September and that an attempt will be made to restore at least some of the money cut from the Health, Education, and Welfare budget by the White House.

Both Senators indicated that a major fight on the issue is in the offing.

CANCER BREAKTHROUGH?

Unfortunately, several misleading statements have been disseminated by the news media concerning bacillus Calmette-Guerin. The bacillus Calmette-Guerin (which is referred to as BCG) is not a new approach to the stimulation of the immune system, since it has been known for at least 13 years that bacillus Calmette-Guerin can stimulate resistance against the development of tumors in experimental animals. However, it is not now ready for general use in human cancer.

In laboratory studies with animals having an early stage of cancer, treatment with bacillus Calmette-Guerin has caused tumor regression in 50 to 75 percent of the animals. Bacillus Calmette-Guerine has been used clinically in a few patients with breast cancer, childhood leukemia, malignant melanoma, and some cancers of the connective tissue. Preliminary analysis of ongoing trials indicates that in disseminated malignant melanoma, treatment with bacillus Calmette-Guerin or with bacillus Calmette-Guerin plus chemotherapy leads to a decrease in relapse rate and an increase in survival. Studies of the injection of bacillus Calmette-Guerin and similar agents directly into tumor masses continue to show that these treatments destroy most injected tumors. Only rarely, however, is there disappearance of uninjected tumors or distant metastases.

The National Cancer Institute will continue to support research into the possible effectiveness of bacillus Calmette-Guerin and related products in the therapy of cancer. The results obtained to date, while encouraging, do not represent a major breakthrough. Also, the results provide a basis for further experiments to determine the circumstances under which clinical benefit can be derived from the administration of bacillus Calmette-Guerin to cancer patients.

[From the National Enquirer, Nov. 19, 1972]

CANCER BREAKTHROUGH?

ENQUIRER IN-DEPTH PROBE—PART 2

Is a cancer breakthrough near? A spark of hope has been ignited for millions of people living with the fear or pain of cancer—because of a vaccine called BCG.

BCG has been yielding such dramatic results in experiments that the National Cancer Institute at Bethesda, Md., recently sponsored a high-level, 2-day meeting of 72 cancer experts from all over the world to confer on the therapy and study the evidence.

The Enquirer was there—with a team of seven staff reporters headed by article editor Iain Calder. The reporters—Bob Smith, Ron Cocking, Bill Burt, John Harris, Tina Langleben, Harold Lewis and Rod Barrand—covered every session of the history-making conference, spoke to 61 of the experts, and came up with heartening news. Many of the specialists called BCG 'a breakthrough"; even more stated flatly that the vaccine is keeping patients alive who would otherwise be dead of cancer.

Last week we told how 5 of 19 patients with severe skin cancer were helped by BCG—of an announcement that BCG was "100 percent effective" against cancer in animals—and of a top researcher's prediction that newborn children may soon be vaccinated with BCG routinely against cancer.

This week we continue the existing BCG story—with news from Canada and France on how the vaccine therapy is saving lives.

TWO CANCER SPECIALISTS HAIL BCG THERAPY AS "A STAR OF BETHLEHEM"

Two leading Canadian cancer specialists, despite professional caution, hail BCG therapy in such terms as "a Star of Bethlehem, a light to be followed" and a "very big step . . . to finding a cure for cancer."

These dramatic statements—matching in enthusiasm those of U.S. doctors who have worked with BCG—emerged in an informal, off-the-cuff discussion between Enquirer reporters and Drs. J. W. Thomas of Vancouver and Harold Taylor of Ottawa, in Bethesda, Md., to attend the international conference.

Dr. Thomas is a hematologist (blood specialist) at Vancouver General Hospital, British Columbia. Dr. Taylor is director of the personnel program division of the Medical Research Council in Ottawa, the Canadian capital.

An Enquirer reporter asked:

"Has there been much BCG research activity in Canada?"

Dr. Taylor replied: "Very much indeed. In fact, Canadian experts have already met to discuss the subject in Ottawa, with about 30 doctors present. The concensus was that there was still a fair amount of basic research to be done before we can really launch into a nationwide clinical trial with BCG. That's my opinion, too, but I'm a bit of a doubter.

"Dr. Thomas, on the other hand, is a believer. He's really enthusiastic about the success he has had in his BCG research in Vancouver. He's doing some great things with it in British Columbia."

Said Dr. Thomas: "In a nutshell, I've been engaged in BCG research for the past 3 years, involving two different kinds of cancer in human patients. But I'd rather not get specific at this stage."

How important is BCG to cancer research at the moment in terms of a breakthrough?

Dr. TAYLOR. Well, I'm the skeptic, but I believe the future looks very promising. At the moment BCG is a Star of Bethlehem . . . light to be followed, a goal to be reached.

It's got to be a breakthrough. It's an exciting new avenue of research which will have to be thoroughly explored.

Dr. THOMAS. Yes, we must be careful to stress that while treatment with BCG is a breakthrough, it warrants careful further evaluation.

Dr. TAYLOR. Don't run away with the idea that we are talking about a cure here.

Having listened to more than 30 experts talking about this subject in Canada, I'm in no doubt that there are many people alive today who would have been dead if they had not had BCG treatment. But they're not cured. There is not sufficient evidence yet to state categorically that a cure has been achieved.

But BCG does arrest cancer. And Dr. Thomas is sure that we're not far away from a cure for cancer.

How far away?

Dr. Thomas refused to make an exact forecast. He said instead: "I wouldn't like to go on record as saying BCG is a cure—but it's one very big step along the medical path to finding a cure for cancer."

FORTY CHILDREN WITH ACUTE LEUKEMIA ARE ALIVE TODAY BECAUSE OF BCG VACCINE, SAYS CANCER EXPERT

Forty children who faced almost certain death from acute leukemia—a deadly form of blood cancer—are alive today because of MCG vaccine, says a top cancer expert.

Dr. George Mathe, head of the Institute of Cancerology near Paris, France, and a pioneer in BCG treatment, told The Enquirer of the results he has obtained with the vaccine.

"Using BCG, 40 of our last 100 patients have been kept alive for a period of 4 to 5 years," Dr. Mathe said in an exclusive interview in Paris. "Using chemotherapy—treatment with toxic drugs—and radiation alone, only about two patients could have been expected to live 5 years."

U.S. National Cancer Institute statistics show an even lower survival rate under conventional treatment, The Enquirer learned. Institute figures indicate that only one to five out of 100 acute leukemia patients live for 3 years, and only one or two out of 100 survive for 5 years.

Dr. Mathe said the majority of his patients are under 15. They come from all over France to the town of Villejuif, where the government-supported Institute of Cancerology is located. A few patients come from the United States after desperate appeals from Americans who have heard of Dr. Mathe's work.

The BCG treatment of the 100 acute leukemia patients came after successful results in earlier clinical trials with BCG.

"We began treating the first of 20 patients with BCG in 1964," Dr. Mathe said. "At the same time we were treating 10 other patients with chemotherapy plus radiation. Those 10 patients relapsed after 130 days.

"Seven of the first 20 given BCG therapy are still showing no signs of the disease.

"One patient has lived 7½ years."

Although his patients have survived far beyond all statistical expectancy, Dr. Mathe will not use the word "cure"—only "cure expectancy."

"It's wonderful to see these patients alive," he said. "And we never stop treatment, regardless of their condition."

BCG—bacillus Calmette-Guerin, named after the two scientists who discovered it 50 years ago—has been used for some years to inoculate against tuberculosis.

To make the anticancer vaccine leukemia cells are taken from patients suffering from the disease, Dr. Roy S. Weiner, an American associate of Dr. Mathe, said, and then weakened by radiation.

When BCG is mixed with these weakened leukemia cells the resulting mixture stimulates the body's natural defenses, which then attack the active leukemia cells in the patient—"killing every last one," Dr. Weiner stressed.

"Chemotherapy alone cannot do this," he said. "No matter how many or how few leukemia cells are present, chemotherapy will kill only 90 percent. Even 10 cells left in the body will cause a relapse, because they will multiply at a rate of from 100,000 to 1 million a day."

But chemotherapy is used on patients before Dr. Mathe begins BCG treatment, in order to lower the leukemia cell count in the body. If the cell count is too high, BCG won't work. When the cell count has been brought down to an acceptable level, Dr. Mathe explained, a solution of the BCG containing weakened leukemia cells is injected once a week.

Patients undergo intensive treatment for 6 to 8 months, and are allowed to go home once it's effective. They return to the Institute every 3 months for a checkup and further treatment.

CANCER VICTIMS URGED TO SEEK SPECIALISTS PROMPTLY; SPECIALIZED CANCER AID ADVOCATED; GAINS IN CANCER PROGRAM UNDER 1971 ACT ARE HAILED

The successful management of patients with cancer depends on the prompt application of increasingly sophisticated techniques of diagnosis and treatment since the information, facilities and special skills necessary to insure provision of the best care are not commonly available outside large medical institutions. There is an increasing need to create channels through which primary care physicians in smaller communities can draw on these highly specialized resources.

Recognizing these needs, the NCI is establishing a system of comprehensive cancer centers which through demonstrations and educational activities will enhance the capabilities of the surrounding medical community. Moreover, the Institute is striving to develop linkages through which the capabilities and experience of multidisciplinary research groups, as well as from other specialized centers and hospitals, can be fully utilized in placing at the disposal of all physicians the information, skills, materials and facilities required to provide the best care for cancer patients.

[From the Washington Post, Mar. 25, 1974]

SPECIALIZED CANCER AID ADVOCATED

ST. AUGUSTINE, FLA., March 24.—The man President Nixon picked to oversee the war against cancer today advised Americans diagnosed as having cancer to seek treatment from medical centers that specialize in caring for cancer patients.

In his statement at an American Cancer Society seminar for science writers. Benno C. Schmidt allied himself with a growing number of cancer specialists who believe that the treatments that can cure some types of cancer and lengthen the survival time of patients suffering from other cancers are so complicated that the average doctor or hospital cannot manage them. Schmidt is Wall Street investment banker who heads the President's cancer panel.

Cancer specialists, for example, now say they can cure with the aggressive use of combinations of powerful drugs more than 50 percent of children suffering from acute lymphocytic leukemia and with radiotherapy 80 percent of the patients suffering from earlier stages of Hodgkin's disease.

Yet only half the patients suffering from those two cancers get the best treatment available, Schmidt said.

And Dr. Justin J. Stein added, "approximately 109,000 cancer patients die annually in this country who could have been saved by earlier and better treatment." Stein of the University of California at Los Angeles, is the new president of the American Cancer Society.

That is almost one-third of the 355,000 Americans who die each year from cancer.

"In my opinion," said Schmidt, "the best cancer treatment today is likely to be a combination treatment only available in certain selected institutions."

"If I had cancer," he said, "I would go to a medical center that specializes in cancer treatments. I would not regard any of them (the different forms of cancer) as small enough that I would not seek the very best.' While saying that, Schmidt would not go so far as to tell Americans not to allow their family doctors to treat cancer cases.

The National Cancer Institute lists 12 centers specializing in comprehensive cancer treatments. By next July, the Cancer Institute expects to add six more centers to its list.

That will mean that more than half of the American people will live within daily commuting distance of a specialized cancer treatment center. Presently, with the 12 centers in existence 52 million Americans live within 60 miles and 90 million Americans live within 120 miles of a treatment center, according to Cancer Institute figures.

Schmidt said that Americans showing warning signs of cancer should see their family doctors, who should realize whether they can successfully treat the case or whether they should refer it to a specialized center.

Dr. Guy Newell, Deputy Director of the Cancer Institute, said the Government is prepared to give doctors and patients names of centers, names of groups of doctors doing clinical studies on cancer, names of cancer control programs, and names of cancer specialists at the National Institutes of Health clinical center in Bethesda who can advise the family physician.

Asked whether the Government should force family doctors to refer cancer patients to specialized centers, Schmidt replied. "It's an explosive political issue. We may get further by not imposing a totalitarian system on our medical men."

Traditionally in American medicine, once a doctor is licensed to practice he can treat any case that comes his way. There are no requirements, except those set privately by hospitals to control the use of operating rooms and other specialized facilities, that restrict the average doctor from treating complicated cases that require specialized care.

[From the New York Times, Mar. 25, 1974]

Gains in Cancer Program Under 1971 Act Are Hailed

St. Augustine, Fla., March 24.—The President's Cancer Panel, emphasizing that the National Cancer Act of 1971 was not a "Manhattan Project" to conquer cancer, said today that the program had nonetheless already resulted in substantial gains in research, treatment, and detection of a wide variety of cancers.

"No one expected that this program would solve the cancer problem in breakthrough fashion," Benno C. Schmidt, president of the three-man panel, told the American Cancer Society's seminar for science writers. "What we did believe is that such a program and more than $500-million a year could make a lot faster progress than the $185 million the Government spent on cancer research in 1970."

Mr. Schmidt, a Wall Street investment banker who is chairman of the board of Memorial Hospital for Cancer and Allied Diseases in New York, asserted: "Cancer is many different diseases, and it is highly unlikely that any single miracle discovery will provide an answer. It is a long-term problem that needs a long-term commitment, and we will be working on some aspect of the problem for many years to come."

Another member of the panel, Dr. Ray David Owen, professor of genetics and zoology at the California Institute of Technology in Pasadena, said that the continued development of "rational, effective cancer therapies will depend on new things coming out of basic research."

However, Dr. R. Lee Clark, the third panel member who is president of M. D. Anderson Hospital and Tumor Institute in Houston, said: "If what we already know about early diagnosis and proper treatment were generally applied, at least one in two cancer patients could be saved—double the current cure rate."

A major problem in improving the cancer cure rate (currently, 355,000 Americans die of cancer each year) is getting patients in touch with the most effective treatment for their particular disease, the panel members said.

Under the Cancer Act, Mr. Schmidt said, there has been an accelerated development of effective treatment for certain cancers, among them acute lymphocytic leukemia in children.

OVER HALF CURED

"We're getting what appears to be cures in better than 50 percent of cases," he said.

However, if children with this disease at first receive the wrong therapy and the disease recurs, the chances of cure are greatly reduced. Currently, Mr. Schmidt estimated, 50 percent of children with acute leukemia are getting optional treatment, whereas 3 years ago only about 15 percent did.

"We are in the process of creating cancer centers all over the country which carry with them the message that they are the places to go in order to get the best treatment," he said. Twelve comprehensive cancer centers exist, nine of them established since the Cancer Act took effect.

Plans now call for an expansion to 35 such centers, to bring modern cancer therapy within daily commuting distance of 80 percent of the population.

In addition, there are about 40 specialized cancer centers around the country, 27 programs have been set up with the American Cancer Society to detect breast cancer in its early, most curable stages, and four study programs are investigating early detection of lung cancer.

Dr. Guy Newell, deputy director of the National Cancer Institute, which administers the Cancer Act, said that persons seeking optimal therapy can write to the Office of Communications, Building 31, Room 10A23, National Cancer Institute, Bethesda, Md., 20014, for the names of cancer programs in their areas. The family doctor may also write to that address for consultation with a cancer institute physician or referral of his patient to a clinical center.

Last year, Dr. Newell, said, the office received 18,000 such inquiries, which are generally answered within 10 days.

[From the Washington Star-News, Mar. 25, 1974]

CANCER VICTIMS URGED TO SEEK SPECIALISTS PROMPTLY

(By Judith Randal, Star-News staff writer)

ST. AUGUSTINE.—More than 100,000 American cancer victims a year might be saved from death if they seek out the best diagnostic and treatment methods available instead of relying entirely on their personal physicians, according to two members of the panel that oversees President Nixon's war on cancer.

"We are saving only one in three cancer victims at present, but we could save one in two if we could get people to better treatment and earlier diagnosis." Dr. R. Lee Clark told science writers at an American Cancer Society meeting here yesterday.

Clark, president of the M. D. Anderson Hospital and Tumor Institute in Houston, is the physician who serves on the three-man presidential board.

Benno C. Schmidt, a New York City investment banker who is chairman of the presidential panel, termed the quality of cancer care "an extremely explosive political issue" since a physician is licensed to treat all kinds of illness whatever his training and experience may be and some doctors are reluctant to give up this privilege.

However, Schmidt also indicated that if he were to develop cancer he would seek out a specialist. "I'm not going to say cancer should never be treated by a family doctor, because there are innumerable people who are alive today after cancer treatment by a nonspecialist," he said. "But no cancer is so small that it need not be checked out by the best person available."

"The primary physician should know his limitations and how to get his patient to the best medical care available," he said. "This means, too, that the specialist should know his limits and not initiate inappropriate treatment. Radiation, for instance, rather than surgery or drug therapy.

Central to the problem is the fact that many forms of cancer require complex therapies and that if these are not given in the first place, there may be no second chance—even if the patient eventually gets the most sophisticated care.

For example, more than 50 percent of the children who develop acute lymphocytic leukemia are alive and well 5 years later if they are treated from the outset with carefully scheduled combinations of drugs and radiation to prevent spread to the brain.

But if they are treated, as many physicians treat them, with only a single drug, there is little or no chance that these measures can be instituted successfully later on and almost no chance of survival.

Patients and their doctors who wish such advice or consultation, they said, should write to the Office of Cancer Communication at the National Cancer Institute, Room 10A23, Building 31, Bethesda, Md. 20014.

UNORTHODOXY GIVEN A TRY

Recent newspaper reports on the testing of Laetrile by the Sloan-Kettering Cancer Research Institute, suggesting that Laetrile had some anticancer activity in animals, have been based on preliminary data and cannot be considered conclusive. Studies must be repeated and verified by other scientists before a drug can be administered to human cancer patients.

The National Cancer Institute has also conducted extensive investigations into the possible value of Laetrile in treating cancer. In the most recent series of tests, conducted between 1969 and 1973. Laetrile was tested in animal tumors and found inactive against the four animal tumor systems in which it was tested. These tests confirm the results obtained in the Institute's earlier tests.

Should the investigators at Sloan-Kettering Institute or any other research institution, however, show through appropriate testing that Laetrile is of value in the treatment of animal tumors, and should its effectiveness then be confirmed through clinical trials in human cancer patients, this development would indeed be welcomed by this Institute, as well as by the cancer patient and his physician.

I believe the most distressing feature of the current Laetrile situation is that it is being made available to the accompaniment of claims that have not been documented in an objective fashion. Such claims suggest to the often frightened and confused patient that a simple solution to this problem can be readily obtained and that he can avoid the sometimes unpleasant realities of surgery or X-ray and hospitalization. Thus, it is not always the patients who have far advanced disease that seek Laetrile and other unproven methods, but also those who could obtain cure or meaningful palliation at an early stage of cancer from well-characterized therapeutic techniques. Tragically, such patients stand to miss their only opportunity for benefit.

[From the Washington Star-News, Dec. 17, 1973]

UNORTHODOXY GIVEN A TRY

(By Judith Randal)

Some call it Laetrile; others amygdalin. By either name it's made from apricot pits and, in the lexicon of orthodox cancer therapists, both terms are dirty words. Among those not of this establishment, however, are hordes of true believers who constantly write to newspapers, and whoever else they think might listen, about the "villainy" of the Federal Government and the American Cancer Society for branding this "cancer cure" as illegal "quackery."

That, at least, is how things stood until the war on cancer got underway 2 years ago and Wall Street investment banker Benno C. Schmidt became chairman of President Nixon's Cancer Advisory Board. Then—according to a recent issue of Science Magazine—Schmidt, who also happens to be on the board of the Sloan-Kettering Cancer Research Institute in New York, began to be deluged with mail about Laetrile, too, and started making inquiries.

What he found was that the drug was indeed held in low repute by scientists, but that their opinion was in part based on prejudice. To make a long story short, Schmidt persuaded Sloan-Kettering to conduct rigorous animal experiments with Laetrile and interested one of its most eminent scientists, Dr. Lloyd J. Old, in personally supervising the job.

As it happens, Old and his colleagues had already tried Laetrile on dogs with naturally occurring tumors and found that it did little good. But in reviewing their data, they decided that the dosages might have been too small and so were eager to probe further on the grounds that—even if amygdalin itself had little to offer in the way of cancer therapy—they might learn something from its study.

This is where matters stand as far as the dogs are concerned. Meanwhile, however, work has gone forward on strains of inbred mice that spontaneously develop breast tumors. The results are initially promising. In one set of experiments, primary tumors treated with Laetrile grew far more slowly on the average than those of their untreated counterparts and in a second study the drug seemed to have some value in preventing the occurrence of secondary tumors in the lung.

Although these results could not be duplicated when the experiments were repeated, Sloan-Kettering—which is also looking into a number of unorthodox treatments besides Laetrile—feels that this lead is still worth pursuing.

What is needed to demonstrate the efficacy of Laetrile—or for that matter any treatment for any disease—is a series of controlled studies in which first experimental animals and then patients are sorted into pairs matched for conditions, ages and other variables. In the animal studies of this kind, one member of each pair is treated with the therapy in question and one is given dummy treatment, alternative treatment or no treatment at all.

In human studies the same philosophy prevails. But, in addition, neither the patient nor the doctor directly responsible for his care knows what treatment the patient is receiving. By this "double-blind" method, "bias"—the opinion or subjective judgment of anyone directly involved in the experiment—is eliminated and only the objective fact remains.

Harsh as this may seem to cancer patients and their families, who understandably are ready to grasp at any straw, it is really the only way to distinguish between a drug whose alleged value is spurious and one whose reputation for value is deserved.

It is agonizing, of course, for the thousands for whom time is running out that such testing must proceed on a step-by-step basis and cannot be done overnight. But it should comfort them to learn that the scientific community is evidently now willing to give unorthodox remedies a fair trial so that the public can have the reassurance of knowing that no stone will be left unturned.

NEW DRUG FOR LUNG CANCER SEEN

The value of the use of an "antagonist," the chemical opposite of a cancer drug, to minimize toxicity from that drug has been recognized for many years, and drug antagonists are therefore quite often given in conjunction with the infusion of a cancer drug. The use of large doses of anticancer drug, methotrexate, and its antagonist, citrovorum factor, in treating lung cancer was first documented by Dr. Isaac Djerassi in the 1960's. Since that time, researchers at the Children's Cancer Research Foundation in Boston, Mass. have published results of studies documenting the even more successful use of methotrexate and citrovorum factor in treating osteosarcoma, a type of cancer of the bone. Further clinical studies being conducted by other investigators and by this Institute have continued to confirm that the combination of methotrexate and citrovorum factor is clearly of value in the treatment of osteosarcoma. The use of this therapy as a prophylatic following amputation for bone cancer is also being explored in clinical studies at this time. Investigators administering methotrexate and citrovorum factor for this purpose have reported that this regimen has produced some very encouraging, but not definitive results. These preliminary findings no doubt provide the basis for the decision to give this treatment combination to Edward Kennedy, Jr.

[From the Washington Post, Mar. 24, 1974]

NEW DRUG FOR LUNG CANCER SEEN

(By Stuart Auerbach, Washington Post staff writer)

ST. AURUSTINE, FLA., MARCH 23.—The new type of drug treatments being given to Edward M. Kennedy, Jr., to prevent recurrence of his bone cancer may work even better in treating lung cancer, the Nation's No. 1 cancer killer, a cancer researcher said here today.

Dr. Isaac Djerassi said he has used the treatment on 10 patients whose lung cancer was so bad that they couldn't be operated on normally and would be expected to die within a year.

After Djerassi's treatment, however, all the patients lived more than 1 year, and one patient is still alive 40 months after treatment started.

Djerassi, director of research hematology at Mercy Catholic Medical Center in Darby, Pa., told an American Cancer Society seminar for science writers that this same treatment could be applied to patients who can be operated on for lung cancer. Even after surgery, about 70 percent of those patients die.

The treatment involves giving the patients a powerful antitumor drug called methotrexate in lethal doses 200 times greater than normal. This drug is then followed by a specific antidote to the methotrexate, citrovorum factor.

Teddy Kennedy, the 12-year-old son of Senator Edward M. Kennedy (D-Mass.), is receiving these treatments every 3 weeks at Boston Children's Hospital to increase the chances that his bone cancer will not recur.

MARROW: A LEUKEMIA NEMESIS

Research on bone marrow transplantation for the treatment of acute leukemia has been part of the Institute's overall attack on leukemia since 1968, and is now one of the programs administered by the Institute's Pediatric Oncology Branch in the Division of Cancer Treatment. Through this research effort, still in its exploratory stages, the Institute is working to develop optimal regimens for preparing the patients for bone marrow grafts, including immunosuppression techniques, and development of effective chemotherapy to eliminate all cancer cells present in the patient's own bone marrow.

Bone marrow grafts have been successfully performed in several centers, as well as here at the National Cancer Institute. Long-term remission from acute leukemia has been achieved by Institute clinicians in 25 percent of the patients treated with this procedure, many of whom had previously responded poorly to chemotherapy alone. One problem encountered in many of the patients receiving bone marrow transplants has been an immunological reaction known as graft versus host disease, a condition in which the transplanted bone marrow produces white blood cells which consider the recipient's cells to be foreign substances and attacks them. Infections during the period of grafts versus host disease have proved to be a serious threat to the lives of approximately 25 percent of bone marrow transplant recipients. Research, however, is being conducted to find ways of controlling these infections, such as development of an antilymphocyte serum and use of germ-free environments.

The use of bone marrow transplantation as a treatment for acute leukemia appears to hold great promise; and as the problems associated with graft versus host disease are solved, this procedure may well prove to be one of our most valuable tools against this form of cancer.

[From the Washington Post, Mar. 26, 1974]

MARROW: A LEUKEMIA NEMESIS

(By Stuart Auerbach, Washington Post staff writer)

ST. AUGUSTINE, FLA., MARCH 25.—Tammy Terkle is 18 and about to graduate from John F. Kennedy High School in Seattle. Two years ago, when drug treatments failed to cure her leukemia, doctors gave her a month to live.

As a last resort, she was given a bone marrow transplant—replacing her marrow, which produces blood cells, including the cancerous white cells that leukemic patients have, with healthy marrow from her younger brother.

Her doctor, E. Donnall Thomas of the University of Washington School of Medicine, cited Miss Terkle today at an American Cancer Society seminar for science writers an an example of the increasing success he is having with bone marrow transplants in patients afflicted either with leukemia or aplastic anemia, a noncancerous disease where the bone marrow stops producing blood cells.

During the past 4 years, Thomas said, he has done 130 transplants; he has a 50 percent survival rate with aplastic anemia patients and a 30 percent survival rate with leukemia patients.

But, he added in an interview, patients whom he has transplanted recently have a far greater survival rate than the eariler transplant patients. For example, of the last 35 leukemia patients who received transplants, only two suffered new cases of the cancer.

Moreover, he said, the doctors have learned to control bacterial infections that once killed patients in the first month after the transplant; in the first half of 1973, he said, no patients died from bacterial infections.

Thomas' basic problem is keeping the patient's defense mechanism from rejecting the transplanted marrow as a foreign substance. Although bone marrow, which forms the white blood cells that are one part of the defense system, is out of commission, the other defense mechanism set up by the lymph glands is still working.

To prevent rejection, Thomas needs a perfect match on four key immunological points—a better match than is required for kidney and heart transplants. While a bad match in those cases might cause the body to reject the transplanted organ, in bone marrow transplants, rejection means the new marrow fights the body and eventually kills the patient.

The best of all possible matches is between identical twins, who make up Thomas' longest living survivors. Three patients even predate the latest series of transplants, with 12-, 8-, and 6-year survival times.

In leukemic patients, Thomas must kill all the bone marrow, with the cancerous cells, before he does the transplant. He uses a powerful anti-tumor drug followed by whole body radiation to do this.

Aplastic anemia is an uncommon disease in adolescents or young adults where the bone marrow stops producing blood cells. About 600 cases of it occur each year in the United States, and there is no satisfactory treatment for it. Thomas said it is often caused by exposures to drugs or insecticides.

While one form of leukemia—acute lympocytic—can now be treated successfully in at least half the cases with combinations of powerful drugs, there is no recognized effective treatment for acute myelogenous leukemia.

After 3 months of drug treatment for acute myelogenous leukemia failed, Miss Terkle was referred to Thomas, who replaced her marrow with marrow donated by her 14-year-old brother. (Bone marrow regenerates itself in a normal person.) She spent the first 100 days after the transplant in the hospital, isolated and masked to prevent infection. Then she moved to a nearby apartment while she gradually regained normal activities.

ZINDER REPORT

Mr. Flood. Let's take a look at the Zinder report which was mentioned in the newspapers after your last advisory board meeting. The subject of that report was the special virus program, is that right?

Dr. Rauscher. Yes, sir.

Mr. Flood. When did that program begin?

Dr. Rauscher. The program began in 1965 with a special appropriation of $10 million initiated and appropriated by the Congress for the purpose of planning and launching an intensified coordinated program of research on viruses and leukemia and related diseases. The Director was advised by scientists both within and outside of the National Cancer Institute that the time was appropriate to launch this kind of program.

Mr. Flood. Was that before you became Institute Director?

Dr. Rauscher. Yes, sir. I became Director of the National Cancer Institute in May 1972.

Mr. Flood. Was it before the conquest of cancer program began?

Dr. Rauscher. Yes, sir. The present cancer program began at the time of the National Cancer Act of 1971, dated December 23, 1971.

Mr. Flood. On what date approximately were you ordered to begin the Zinder study? Who ordered you to do it?

Dr. Rauscher. This is a study that I called for myself. I spoke with several members of the National Cancer Advisory Board who in turn recommended to the Chairman of the Board, Dr. Jonathan Rhoads, that this study be undertaken. The Board members concurred and the study was actually begun approximately 1 year ago. I might add, Mr. Chairman, that this study is similar to others that I've requested or that the Board has requested and which are currently ongoing. For instance, the programs that deal with chemical carcinogenesis, organ site task forces and others are currently being reviewed by ad hoc subcommittees of the National Cancer Advisory Board. I believe that this is good management and in addition it keeps the scientific communities of this country informed as to major activities within the national cancer program.

Mr. Flood. Would you then call it an exercise in self criticism?

Dr. Rauscher. Yes; I would. Certainly it's one aspect of self-evaluation as well as outside peer evaluation of both management and scientific aspects of a particular program.

SPECIAL VIRUS PROGRAM

Mr. Flood. Do you think that the fundamental idea of the special virus program, that is, the gambling that a basic research idea, could be the one to constitute a scientific breakthrough, do you think the fundamental idea is wrong or a misuse of money? Would you do it again?

Dr. Rauscher. Mr. Chairman, I think this is one of the best ways to use funds for disease-orientated research and I would certainly do it again. Perhaps a few additional comments might be helpful in terms of providing a perspective of what was taking place at the time this program was initiated. As I mentioned before, the decision to begin the program was based on much advice from scientists throughout the country as well as from those working within the National Cancer Institute.

At that time there were few top notch investigators willing to work in tumor virology. This was because it was and is a very difficult and complex field and because of the nature of these viruses, experiments could not be finished in less than 1 year. In fact, many experiments took 2 to 3 years to complete in animal systems. One task, therefore, was to encourage people to apply for support through this program for studies that were deemed very promising and very important to the control of these cancers in people. The contract mechanism was used in order to get the program going more quickly. At that time, we were able to award contracts to academic or commercial investigators within about 3 to 3½ months. It took about 9 months to review and award a grant after the investigator wrote his application and submitted it to the National Cancer Institute. We were also encouraged to support research and development investigators in private commercial laboratories. Then and now the contract is the only mechanism that can be used to support such investigators in these laboratories. It was hoped at that time that viruses could be isolated from children with leukemia similar to the more than 30 viruses already known to cause leukemia and other cancers in laboratory and domestic animals. We now know that that hope was overly optimistic and that the probable virus etiology of some human cancers is far more complex than the simple isolation of the causative virus. I should add that to a very large extent it is because of the work performed by investigators in this program that we now know that other approaches must be used to determine whether viruses are causative of human cancers. So in this regard, the program has been very successful and I believe continues to be. One more very important factor. The program was started not only to exploit existing information through a targeted coordinated effort, but also to generate and expand the base of fundamental information so that additional advances could be made toward the control of these diseases in people. I believe that this has been done very well.

Mr. Flood. Is that what you call targeted research?

Dr. Rauscher. Yes, in the sense that projects of the highest apparent priority are supported through a coordinated effort toward the control of a particular disease.

Mr. Flood. Is your interpretation of the National Cancer Law one that envisions such gambles? Does all fundamental research involve such gambles?

Dr. Rauscher. I think the word gamble is an excellent one and can be applied to all research whether it's fundamental or applied. This program was and continues to be an excellent gamble in the sense that it has enormously broadened the scientific base of information and, therefore, our understanding of the disease process. It has not yet resulted, however, in the control of these diseases, but I am confident that this will come.

Mr. Flood. When did you first begin to get the findings of the Norton Zinder Committee?

Dr. Rauscher. The first report was made to the National Cancer Advisory Board in November 1973. The Board requested additional information and clarification of some of the issues raised in the preliminary report. It was agreed that the final report be submitted to the Board at its meeting in March 1974.

Mr. Flood. When did you begin to shape an answer to the problems it raises?

Dr. Rauscher. Both management and scientific aspects of this program were under review and were being modified at least several months prior to the submission of the preliminary report in November 1973.

Mr. Flood. Do you think the main thrust of the report was correct?

Dr. Rauscher. I think the report is essentially a good one. To some extent it is based on a dislike and misunderstanding of the contract mechanism. But of course, this is our problem; we must do a better job of informing the scientific community as to how and why and when the contract mechanism is used. As you know, a major issue in the report is the feeling that contracts do not receive the same high quality peer review that is true of the grant mechanism. The committee was concerned that the program was not open to optimal competition and to objective study section-like review. In other words, they want to be sure that management aspects of the program are completely separate from the peer review process. I agree with their concern and the Institute has already taken steps to assure this separation and to assure that the program is totally open to competition of new ideas and to the best peer review mechanism available. I might also point out that, because of the scarcity of qualified and interested investigators when the program started in 1965, it was inevitable that sooner or later people who were doing the work as contractors would also be reviewing the work as members of review committees. Now that there are many qualified investigators interested in this area of cancer research, this duality of functions need no longer exist.

Mr. Flood. Do you think the remedy is now in place?

Dr. Rauscher. Mr. Chairman, I assure you and members of the committee that all modifications of this program as recommended by the Zinder committee and endorsed by the National Cancer Advisory Board will be implemented in the near future. Mr. Chairman, if I may, I would like to submit as an addition to the record a summary of the major progress highlights that have occurred through this program since it began in 1965.

[The information follows:]

HIGHLIGHTS OF SPECIAL VIRUS CANCER PROGRAM SINCE 1965

In 1911, Peyton Rous identified the first cancer virus in solid tumors of chickens. In spite of this discovery, research on viruses and cancer was delayed for 40 years because Rous' experiments were not always reproducible, and scientists were not able to isolate or grow the virus in a laboratory. In 1936, John Bittner discovered a virus-like agent in mouse breast cancer, but the scientific techniques necessary to confirm that agent as viral were not developed until years later.

In the early 1950's, Ludwik Gross discovered the mouse leukemia virus. Seven years later, a second virus was recovered and grown from mouse cells in which it was obscuring experiments on the leukemia virus. This second virus, polyoma, caused 26 types of cancer in mice, a phenomenon that awakened vast interest in viruses as possible causes of human cancers.

By 1964, there was increasing worldwide concern that viruses similar to those which caused cancers in animals might also cause human cancers. Circumstantial evidence suggested a viral cause of leukemia in cattle, and NCI scientists received reports that leukemic dairy cows were being killed by Danish farmers who feared transmission of the disease through milk or other dairy products.

A scientist in Scotland reported isolation of an RNA virus from leukemic cats, and several laboratories reported finding particles in human leukemias and lymphomas which resembled RNA viruses (those containing an hereditary core of ribonucleic acid) known to cause animal leukemias. Scientists in England reported isolating a DNA virus (containing a hereditary core of deoxyribonucleic acid) from patients with Burkitt's lymphoma, and small clusters of human leukemia (suggesting an infectious agent such as a virus) were reported in three rural U.S. communities.

In 1964, with a special $10 million appropriation from the U.S. Congress, the National Cancer Institute began an intensified research program on cancer viruses. With the advice of leading non-Federal scientists, the NCI defined its major research objectives and outlined the specific projects and resources necessary to accomplish the objectives.

In addition to determining whether viruses cause human cancers and if suitable measures could be developed to control virus-caused cancers, the Institute targeted four major research areas under the new program:

(1) The nature of animal leukemias and their relationships to human;
(2) The hazards of working with viral agents;
(3) Development of animal and cell culture systems, quantities of viruses and other materials needed for research; and
(4) Improved treatment for the disease in humans.

Vast evidence accumulated in the program (and in grant-supported research) suggested that RNA viruses cause many kinds of cancer in a wide variety of animals, particularly in rodents, chickens, cats, and more recently, in subhuman primates. In the extensively studied animal models (chicken, mouse and cat), it is clear that these viruses can cause natural disease. DNA herpestype viruses are similarly associated with natural cancers of animals and man.

Although candidate human cancer viruses have been isolated more frequently in recent years, none has met the rigorous criteria necessary for firm identification as a cause of human cancer. Research findings and the nature of the disease in humans have led to extensive modification of the original goals of the virus program. As a result, scientists have acquired the knowledge, techniques, experimental systems and insight to identify viruses and study their genetics, protein products and other activities inside the human cell.

Many of the early projects concentrated on developing experimental methods and materials necessary to advance virus research. By 1967, new methods to grow the mouse leukemia virus in large quantities necessary for definitive study had been developed. This accomplishment led to development of techniques for growing other needed viruses. For example, cultured Burkitt's lymphoma cells containing the human herpes virus (known as Epstein-Barr virus) were selected, grown in quantity, and made available to scientists. This was the first time that a standardized culture of Epstein-Barr virus was available for scientists to compare research findings. Until then, individual scientists had used various virus cultures, which made it difficult and sometimes impossible to compare research results.

Nine techniques were developed for detecting antibody to Epstein-Barr virus in human populations. Blood samples were collected from patients and normal controls around the world, coded, and sent to contract laboratories for tests using the various techniques. Results were compared, and three of the nine techniques were selected because they were uniformly reproducible, sensitive and least expensive for larg-scale population studies.

The virus cancer program currently supplies research materials of general interest from six local and regional repositories. Materials are sent to scientists under contract and within NCI, and as supply permits, to qualified cancer virus investigators throughout the world. A centralized computerized inventory lists more than 100,000 vials of blood samples from over 15,000 individuals and 3,000 normal and cancerous tissue specimens from 1,000 individuals. Uniformly prepared viruses, cell cultures and viral reagents are also available so that research findings may be compared.

The program has developed necessary safety standards for laboratory workers handling viral and chemical agents. These standards are being developed into an official policy on safety. The program has designed special containment devices necessary for the safe large-scale production of virus materials, developed certification procedures for critical safety equipment, and sponsored safety training courses for scientists and laboratory help. Program leaders frequently have advised institutions planning new or renovated facilities for research.

Over the years, the virus program has reported several important "negative" findings. These lengthy, expensive, but rarely dramatic studies enabled the program to identify research approaches and biological agents that were unlikely to provide solutions to the problem of cancer in man. With this negative information it was possible for the program to rapidly shift research focus into more productive scientific areas. This quick and flexible responsiveness to a rapidly evolving science base prevented continuing expenditures on outmoded research approaches and insured maximum scientific progress for each dollar of funding Some examples:

1. As the result of several studies, scientists in the program determined that mycoplasma, an organism often found as a contaminant of cell cultures and human specimens, does not cause cancerous changes in cells.

2. Several human adenoviruses, which cause mild respiratory disease in humans, were found to cause tumors when inoculated into newborn rodents. Animals bearing these tumors reacted to the virus by producing antibodies to a viral T antigen, or tumor protein. Scientists in the program purified the protein and tested 6,000 human blood samples for antibodies to it.

Results were completely negative. In addition, other scientists, applying a technique known as molecular hybridization, found no similarity between the hereditary information of the virus and that found in the tumor cells. Adenoviruses subsequently were eliminated as causative agents in human cancer.

3. Program scientists were able to verify the presence of viral particles in approximately 30 percent of human leukemic samples studied under the electron microscope. However, they were unable to induce leukemia in approximately 700 subhuman primates inoculated as newborns with human leukemia specimens. Because of their complete failure to transmit leukemia or its "virus" to monkeys by these techniques, scientists in the program were compelled to find new ways to detect virus and its activity in human cells. Techniques were developed to find antibodies to a virus or its products; cell culture techniques were perfected; and biochemical and immunologic techniques were developed for the study of subviral components.

4. Program scientists confirmed the isolation in 1964 of a cat leukemia virus. They demonstrated the ability of the virus to cause cancer in a variety of animals including dogs, cats, and monkeys and showed that the virus could infect human cells grown in culture. Because cats are closely associated with humans, a population study was begun in California in the late 1960's to determine whether cat owners were at higher risk to leukemia than the general population. The study concluded that cat owners have no increased risk of developing leukemia.

5. Because of suggestive evidence that leukemia in cows might be caused by a virus present in the milk, the virus program sponsored studies to determine the relationship of milk particles to bovine leukemia. By 1968, one of these studies showed that the usual pasteurization methods kill animal RNA and DNA viruses deliberately added to cow's milk. This finding demonstrated that children and adults appear to be at no risk to developing leukemia from milk and milk products which have been pasteurized.

6. The oncogne theory, advanced in 1969 by Drs. Robert Huebner and George Todaro of NCI, and the provirus theory of Howard Temin, McArdle Laboratories, Inc., University of Wisconsin, provided the impetus for major new research within the program on the natural history, immunology and genetics of RNA cancer viruses. These two theories postulated different means by which the RNA viruses could infect and be incorporated into the hereditary information of the cell to cause cancer.

Many interesting findings resulted from work generated by these theories. Following the discovery that certain chemicals can activate RNA viruses in cultured cells, program scientists learned that such endogenous or native viruses, can be activated in many types of animal and human cells. These findings indicate that many cells contain the structural components of the RNA virus in an unassembled form.

The endogenous viruses have not yet shown cancer-causing activity. However, even the limited information gained about them within the virus program helped to identify a candidate human virus as an endogenous, previously undiscovered cat virus. Extensive efforts are underway to isolate similar endogenous viruses from human tissues.

Due to program-sponsored research, substantial evidence has been uncovered that, in animals at least, RNA type-C viruses are transmitted as genes from parent to offspring. Within the past few months scientists have isolated the first native RNA type-C virus from normal baboon placental tissues. Similar virus particles have been observed consistently in normal human placental tissues, and efforts are underway to isolate and grow the virus. Using chemical probes made from the baboon virus, program scientists also are attempting to determine whether the human particles are related to the endogenous baboon virus.

The scientists suggest that their findings may show that type-C virus is a normal phenomenon in the development of the embryo. Alternatively, its presence in the placental tissues possibly was triggered by a hormonal change and could signal hereditary transmission of the type-C virus in primates.

Recent findings by Dr. Sol Spiegelman of Columbia University in New York City cast some doubt on the validity of the oncogene theory, however. Dr. Spiegelman reported this in September 1973, following his studies of the hereditary chemicals in white blood cells from two sets of identical twins. One member of each twin pair had leukemia. By using a molecular probe to assay the hereditary chemical, or DNA, of each twin, Dr. Spiegelman discovered that in each case the twin with leukemia had chemical sequences in his cells related to those of leukemia-causing viruses of animals. The healthy twins' blood cells were free of these virus-related chemical sequences. Since identical twins are produced by the union of one sperm and one egg, each twin would be expected to have the same hereditary chemical characteristics. This was not the case, and Dr. Spiegelman suggested that the chemical aberration in the leukemic twins' DNA resulted from factors affecting the cells after conception or after birth, rather than from an oncogene, or virus gene, present from conception. If this is true, the chances of preventing or curing at least some forms of cancer are significantly improved.

7. Since the discovery of the enzyme reverse transcriptase in 1970 by Drs. Howard Temin and David Baltimore (Massachusetts Institute of Technology), research has accelerated in the field of RNA viruses. The virus program rapidly determined that reverse transcriptase is present in all known RNA cancer viruses. This finding established an association of the enzyme with virus-induced cancers in animals and led to the development of sensitive techniques to detect very low levels of viral activity in human tissues.

Studies on the function of this enzyme continue. However, scientists at NCI recently purified both the reverse transcriptase and hereditary chemicals found in some adult acute leukemic patients. Using newly developed techniques, the scientists found these chemicals to be closely related to similar chemicals in the solid tumor viruses of mice and primates. This is the clearest available evidence of RNA virus activity in human leukemia.

8. In the late 1960's, program scientists identified by electron microscopy particles similar to the mouse breast cancer virus in normal milks of women at risk to developing breast cancer, and in the tumors themselves. Biochemical studies on human milks confirmed this association. Recently, other scientists showed that purified cores of the particles from human milks are chemically related to hereditary chemicals in breast cancer tissues. Despite such developments by program scientists, at the present time a causal role for viruses in human breast cancer cannot be demonstrated.

Other studies within the program have advanced the science of cancer virology in equally important ways. For example, the first evidence that a human virus under some conditions can cause cancerous changes in normal human cells occurred within the program. Scientists showed that normal skin cells from patients with nonmalignant diseases such as Fanconi's anemia and Down's syndrome undergo cancerous changes after infection with common monkey and human DNA viruses (SV40 and human adenovirus). Persons with these diseases have a much higher risk of developing cancer than the general population. The studies confirmed the cancerous potential of DNA viruses under laboratory conditions.

Studies on DNA viruses have concentrated on the known human herpes type viruses—the Epstein-Barr virus strongly associated with Burkitt's lymphoma and nasopharyngeal cancer, and the herpes simplex viruses associated most often with cancer of the uterine cervix in women.

Epidemiologic data developed within the program has strengthened the relationship between the Epstein-Barr virus and Burkitt's lymphoma, although no causal relationship has been established. Immunologic techniques demonstrated high levels of antibody to the virus in patients with Burkitt's lymphoma and nasopharyngeal cancer. Recently, using a new technique, program scientists demonstrated for the first time the presence of Epstein-Barr viral products inside the Burkitt's lymphoma cell and in the surface cells of nasopharyngeal cancers.

Program scientists discovered that lack of a certain immunologic response to the virus in treated Burkitt's patients confers greater chances for survival. They also determined that the virus is the cause of infectious mononucleosis. Hereditary information similar to that in RNA cancer viruses also has been found in Burkitt's lymphoma and nasopharyngeal cancers, suggesting that both types of viruses may be factors in causing these cancers.

Studies on antibody responses to the herpes simplex viruses of man led to discovery within the program of the relationship between the virus, early sexual promiscuity and heightened risk to cancer of the uterine cervix. The studies of scientists within the program such as NIH Fogarty Scholar Albert Sabin and University of Naples' Guilio Tarro suggested that the common herpes viruses may be associated with other types of cancers in humans as well. This work is being continued at the NCI Frederick Cancer Research Center at Fort Detrick, Md.

The recent discovery that a herpes virus harbored by the squirrel monkey can cause malignant lymphoma and leukemia in owl monkeys and marmosets reaffirmed the cancerous potential of these DNA viruses. This was also demonstrated by the finding that human herpes viruses made genetically defective with a simple dye and light inactivation procedure caused cancerous changes in cells.

It has been difficult to prove that under natural conditions herpes viruses cause human cancer. The Epstein-Barr and herpes simplex viruses persist in large segments of the human population for extended periods, and cause various types of illness, possibly including cancer. Whether these viruses, and other human herpes viruses such as varicella and cytomegalovirus, can cause cancerous changes in humans or act in concert with other agents to produce cancer requires additional careful study. New findings in virus research have demonstrated repeatedly the complexity of human cancer. However, with techniques developed within the virus program, scientists can now identify the biochemical and immunologic characteristics of any new virus discovered in animal or human cells. The major internal proteins and the reverse transcriptases of all known RNA cancer viruses have been purified and characterized, and specific viral reagents are available.

Instead of searching for the complete virus in cells, scientists now use these new techniques to search for viral hereditary information, viral reverse transcriptases, and proteins related to known cancer virus proteins. Using chemicals and cell culture techniques, they also attempt to induce the appearance of a virus or its components in human cells.

The activities of the virus cancer program established NCI as the key resource for information on cancer-causing viruses. The NIH Bureau of Biologics has asked the program for advice in monitoring vaccines for potential cancer-causing agents. The Department of Agriculture has designated building 41, NCI's high hazard containment laboratory, as a clearinghouse to identify potentially harmful agents in many of the biological materials sent to the United States by collaborating foreign scientists. The program has worked with the World Health Organization's International Agency for Research on Cancer to plan an international network of reference laboratories which would provide research materials to investigators throughout the world.

In addition, under the U.S.-U.S.S.R. health agreement, U.S. scientists recently helped identify a virus isolated from human cells in the U.S.S.R. The scientists found that the Soviet virus was nearly identical to a virus proviously isolated in the United States from a monkey with breast cancer. The two viruses may represent a new class of RNA viruses with many of the characteristics of known cancer viruses.

Thus, the research, materials and techniques developed in 9 years within the virus cancer program has increasingly contributed not only to U.S. cancer virology, but to interagency and international collaboration. These accomplishments have created an entirely new science base without which the national effort to prevent, cure, and control cancer, could not be sustained. In addition, the virus program and the NCI will continue to serve as a unique resource for developing answers to biological problems of concern to the entire spectrum of biomedical research.

CLINICAL TRIALS

Mr. **Flood**. If you define the subject of the special virus program as basic research, how about clinical research? How much money did you spend last year on clinical trials involving cancer of the colon?

Does that figure cover the cost of drug development? Give it to me without the drug development cost, please.

Would you please give the committee the same figure—the cost of clinical trials without the drug development costs—for all the other organ sites? Please include lung, breast, pancreas, ovary, prostate, stomach, testicle, brain, esophagus, kidney, bladder, cervic, head and neck, and bone.

If there are any others items to be included in clinical costs, please list each one separately and give me your total clinical trial costs for the most recent year on which you have complete figures as well as what you have spent so far in fiscal 1974.

Dr. **Rauscher**. Mr. Chairman, with your permission I will provide that information for the record.

[The information follows:]

CLINICAL TRIALS

[Excluding drug development costs]

Site	1973	Obligations through Feb. 28, 1974	1974 estimate
Head and neck	$2,220	$854	$3,890
Esophagus	634	320	876
Stomach	3,945	2,178	5,279
Colon—Rectum	6,908	3,984	9,334
Liver	4,079	2,550	5,430
Pancreas	1,338	284	1,866
Lung	10,412	7,782	16,594
Bone	1,449	970	1,898
Breast	9,237	6,914	18,966
Testis	940	1,418	3,150
Prostate	1,195	1,467	4,008
Cervix	965	1,559	2,430
Ovary	1,610	2,770	4,727
Bladder	1,524	943	1,986
Kidney and other urinary	899	479	1,809
Brain and CNS	1,786	965	2,282
Leukemias	19,659	9,854	25,174
Lymphomas	11,173	6,985	14,308
All others	11,069	10,742	26,883
Total	91,042	63,018	150,890

INFORMATION ACTIVITIES AND SERVICES

Mr. **Flood**. Your publication, Information Activities and Services of the National Cancer Institute has come to my attention. I am happy that you recognize in print the National Cancer Law's stress on information.

The computerized data banks information is of particular interest. I note that the first deals with anticancer drugs, about 30 percent of which is available on a nonconfidential basis.

The second deals with possible cancer-causing materials and is half-functional, the second half under development.

The 3d, 4th, 5th, 7th, 8th, 9th, 12th, 13th, 16th, 17th, 18th, 19th, 20th are all for communication back and forth among researchers or NCI staff. Some of the others are proposed, essentially inactive, or working tools rather than systems for communication outside of the Institute.

You have made the statement that most letters to the Institute are answered within 10 days. Add mailing time and that makes roughly 2 weeks. Do you consider this fast enough?

Dr. Rauscher. No, we do not, and we are making special efforts to shorten this time lag through expansion and improvement of the Institute's public inquiries operation. Even though most inquiries are answered within 10 days, the Institute does much better with inquiries from patients, who receive top priority. On the average, these letters are answered within 3 days.

The Institute also receives from patients about 1,000 telephone inquiries a year, and these are answered immediately or at least within the same day. Since the telephone provides the most rapid means of response, the Institute is exploring the use of an "800" telephone line which would allow people from anywhere in the country to call toll-free for cancer information.

Mr. Flood. If someone in my family develops an uncommon form of cancer do you have a computer to tell him within a day or two exactly where that type of cancer is being treated intensively?

Dr. Rauscher. The NCI staff responsible for answering public inquiries has computer backup. For example, each staff member has at his desk an up-to-date, well-organized computer printout showing the locations of NCI's treatment research programs by type of cancer, by institution and by physician-investigator. These treatment research programs involve 1,600 clinical investigators at 320 hospitals and other institutions. Last year more than 20,000 patients with the various forms of cancer were treated in these studies, and the physician-investigators used similar treatment methods on a nonresearch basis for countless other patients with the same diseases. In most instances, patients requesting treatment information are given the name, institution, address and telephone number of at least two physicians in their geographic region who are studying their particular kind of cancer. In addition, NCI provides the name, address and phone number of an NCI staff member who will provide free consultation services for the patient's physician.

The public inquiries staff is also able to provide patients with the name of a contact person at all of the comprehensive cancer centers and at institutions which are participating in projects to demonstrate new prevention, diagnosis, treatment, and rehabilitation techniques and services.

PRESIDENT'S CANCER PANEL

Mr. Flood. The chairman of the President's cancer panel was reported in the newspapers recently as saying most cancer patients had better get themselves to a prominent cancer center. He stopped just short of saying that the family doctor might be overtaxed by the cancer problem. What kind of priority do you place on responding by computerized information—I stress the speed of computerized information—to families looking for the best place to send their cancer-stricken relatives?

Dr. RAUSCHER. We place a high priority on systems that feature rapid retrieval of information needed by families and physicians seeking treatment information, and computers will be used whenever feasible. As the program expands, as more institutions become capable of providing excellent cancer care, and as more types of cancer become treatable successfully, it is likely that computers will be the only feasible way to handle the information.

Mr. FLOOD. Is it reasonable for such a family to want to know where the several places are in the United States that specialize in specific types of cancer to get the information in 24 to 48 hours?

Dr. RAUSCHER. I think it is not only reasonable, but necessary—for practicing physicians as well as patients and their families. It also should be pointed out that we are beginning work with the comprehensive cancer centers to help each of them establish programs to quickly handle patient and physician inquiries on a regional basis. This is essential. We must develop a rapid, responsive system as close to the patient and local medical resources as possible.

Mr. FLOOD. Can you now supply to outside inquirers the name of the leading specialists in specific types of cancer—answering within 24 to 48 hours?

Dr. RAUSCHER. If the inquiry is made by telephone, we can identify research specialists for specific cancers. If it is made by letter, our response is mailed, on the average, within 3 days of receiving the inquiry. We are making serious attempts to increase the speed with which we respond to inquiries.

Mr. FLOOD. If a patient hears of an experimental drug seemingly helpful to him, can he find out by computerized information source where the legitimate investigators of this drug work?

Dr. RAUSCHER. The patient and his physician have access to such information through NCI staff, whose data sources include computer-based information.

INTRAMURAL AND EXTRAMURAL RESEARCH

Mr. MICHEL. Last year I asked a question as to what portion of the research in cancer was done in-house and intramurally as against extramurally. I think you said in-house was 10 percent. Would that still hold?

Dr. RAUSCHER. Intramural funding takes about 6.6 percent of the budget. In addition there is another 8 percent used for NCI and NIH management costs. We are talking about 85 percent of the total budget going extramurally.

Mr. MICHEL. Is that good?

Dr. RAUSCHER. I think so. Our costs in-house have not increased nearly at the rate of our expanding extramural activities over the last 3 or 4 fiscal years.

EMPLOYMENT

Mr. MICHEL. How has all this increased funding affected the personnel numbers in your shop? That is not to suggest I would measure the effectiveness of the Institute by the number of people you have working there. I am just rather curious. Is there any significant increase in the number of people employed in the Institute with all this increased funding or is that reflected in additional outside grants or contracts?

Dr. RAUSCHER. We have had significant increases in positions. In 1971 our position base at that time was about 1,430. We expect it will be 1,873 in 1975. The Department provided an additional 100 positions for 1974. We are hoping to get an additional 35 positions in 1975.

Mr. MICHEL. Are these administrators, researchers?

Dr. RAUSCHER. Both categories. About half are used for management, not only fiscal types but scientists whose major job it is to coordinate activities throughout the country. Others are technical positions right on the campus in Bethesda.

RECRUITMENT OF SCIENTIFIC STAFF

Mr. MICHEL. Do you have any trouble recruiting from the scientific community the kinds of people you want for the Cancer Institute?

Dr. RAUSCHER. The answer is yes.

Mr. MICHEL. Why?

Dr. RAUSCHER. It depends on what level. It has been more and more difficult to recruit people at the top because of the fact that salary increases have remained static for about 5 years. We are becoming very noncompetitive.

Mr. MICHEL. Is that the only reason?

Dr. RAUSCHER. We are noncompetitive for key people. I think the research and clinical opportunities we can offer on the campus continue to be as bright and challenging as those provided by any other institutions in the country.

One other aspect of recruiting is that as we develop a larger program wherein we try to effect as good coordination as is possible, more and more I have had to ask some of my key staff to help me in coordinating the management aspect of the program. To some extent this takes some people away from pure research activities. I think this is probably an understandable result of operating a larger program wherein we want to coordinate information throughout the country. It takes people to do that. Some people prefer not to come into that kind of work.

To answer your question, that may be a reason why it is in some cases difficult to recruit. I don't think it is a major reason.

COST OF AVERAGE GRANT

Mr. MICHEL. What is the average research grant for one who is basically in the research area? He has a bug about a new approach. What do we have to spend to honor a request of that kind with no real assurance that it will pay dividends? We know that it is risk money.

Dr. RAUSCHER. That is right. It is about $45,000 for the first year with a moral commitment for 2 succeeding years before the next major review.

Dr. STONE. On your use of the expression "risk money," I sympathize with what you mean. But some of the acquired knowledge is like putting money into the bank. We expect it to be useful some years from now when other accretions of knowledge, other correlations of facts have come about. I would want to be careful about the supposition that the money spent on such research had in any way not been usefully used. It might take two generations before it pays off, but the knowledge is in the bank and will be used in many ways.

CANCER CENTER

Mr. **Michel.** Last year, in speaking of cancer centers, I thought we were talking in terms of perhaps 15 rather than 12. I think your testimony states you will put 12. Why are we short?

Dr. **Rauscher.** My statement last year, which is still accurate, is that before the end of this fiscal year it is likely we will have recognized all 15 newly authorized comprehensive cancer centers. We have recognized 9 new ones plus the three existing, which makes 12. We have six to go to reach a total of 18.

SPECIALIZED CENTERS

Mr. **Michel.** The figure which comes to mind is 47. I specifically asked you—"How about these other 40-plus centers you spoke of in your testimony?" You corrected me and said "47."

Dr. **Rauscher.** Those are the specialized centers, where they specialize in chemotherapy, radiotherapy, or other disciplines.

Mr. **Michel.** Are we up to target there?

Dr. **Rauscher.** Yes.

Mr. **Michel.** Are there 47?

Dr. **Rauscher.** There will be 49 by the end of this fiscal year.

LOCATION OF CANCER CENTERS

Mr. **Michel.** Let me ask again as I did last year—do these centers all tend to gravitate around the existing biomedical research centers?

Dr. **Rauscher.** Pretty much so, yes.

Mr. **Michel.** You may recall that I made the comment that I was reminded of the enactment of the Cancer-Heart-Stroke Regional Medical Programs, the so-called centers which were to be established. Now we find the Department, in effect, saying, "knock out the regional medical programs. Some are good and some are bad.

Then we find here in your shop that you are setting up these centers in the very same places where normally we would have had them under a regional medical program. Is there any contradiction here or any conflict between your position and that of the Cancer Institute with regard to the overall position of the Department regarding medical programs or regional centers or geographical distribution?

Dr. **Rauscher.** I don't think so. We have several approaches we are using. First of all we like to take advantage of the very best institutions in the country. They already have their construction and excellent staffs for working on cancer problems.

We are also trying to go into institutions, such as MIT, which has microbiological and biological departments of great excellence. We are trying to encourage them to work on some molecular aspects of cancer. In fact, they are one of the newest specialized centers.

UTILIZATION OF CANCER CENTERS

Mr. MICHEL. Those persons with adequate means who have some form of cancer in the family have the natural inclination to send their loved one to the best known place they can for treatment. Is that the kind of advice you give to anyone today who has a problem of cancer in his family—we have to get you to one of these specialized centers because that is a technical subject. To go to one with no specialized competence you are shortchanging yourself. Is that a rule of thumb you follow?

Dr. RAUSCHER. It depends on the type of cancer. We answer all inquiries this way—we identify the best hospital, usually a comprehensive cancer center or a hospital engaged in cooperative clinical trials, in that geographic area. We advise on the forms of treatment deemed best by the community of medicine. In some cases we can't advise them as to the best form because we don't know. To the extent we know, we advise.

It doesn't mean that a patient has to be hospitalized immediately within the comprehensive center. A community outreach system is important where the center serves as an information quarterback; 20, 30, 50 institutions may work together. Then the patient can be treated effectively in a smaller hospital.

Mr. MICHEL. Are we giving you sufficient funding for you to advance that concept as rapidly as possible?

Dr. RAUSCHER. At the present time, yes.

ADEQUACY OF BUDGET

Mr. MICHEL. Overall is this budget request adequate—that may be a little unfair. Did you request any more than what you have in the budget?

Dr. RAUSCHER. On advice of the people in the country who are helping with updating of the National Cancer Plan, and the advice I have received from the President's Cancer Panel and National Cancer Advisory Board, they feel that substantially more dollars could be effectively spent. I think the cancer program has been treated very well by the Congress, by OMB and others in recent years. The nature of cancer is such that we will never have enough money to do everything that possibly can be done now. Clearly, as so many others have said, there are other priorities in health. We can spend more money. We can spend more money very, very well. It is a matter of what other competing priorities there are.

Again, in summary, the advice I am getting from major cancer groups in the country is that substantially more funds could be used well. This is true of so many other diseases in the country, of course.

LUNG CANCER

Mr. MICHEL. You spoke of three projects that you started for early detection and treatment of lung cancer in persons of high risk, men 45 to 69 years, who are regular cigarette smokers. How long will these projects run?

Dr. RAUSCHER. The projects will run at least 10 to 15 years.

Mr. MICHEL. Would we be expecting to get intermittent results?

Dr. RAUSCHER. Yes. This is true of any early detection or diagnosis programs. The best we have had for lung cancer up to date has been X-ray scanning.

We now know in some cases that the fiberoptic scope can make possible identification of a cancer lesion 5 years before it shows up as a spot on X-ray. Then we can go in and remove the lesion surgically or treat it in some other way. Depending on the number of patients treated it will take 5 or 10 years to find out whether that procedure has increased survival.

Mr. MICHEL. I assume this work is being done by contract outside?

Dr. RAUSCHER. Contract and grant with outside institutions. We also have a major program ourselves——

Mr. MICHEL. If there are three projects, will there be more than three institutions involved?

Dr. RAUSCHER. Yes. As a matter of fact, there are four because we have our own project with the Veterans' Administration here in the District of Columbia. There will be more, depending on the success we have in using this procedure.

ACCESSIBILITY OF CANCER CENTERS

Mr. MICHEL. When you speak of the 100 million Americans who will be within 60 miles of one of these institutions, would it be your goal that it be increased to 150 million and on up the scale in years ahead?

Dr. RAUSCHER. The figures are roughly like this: When we have established a total of 18 comprehensive centers there will be on the order of 100 million people who live within 60 miles.

In order to cover about 175 million there will be a need for something like 32 comprehensive centers. After that you have to go to something like 50 centers to cover just another 5 million people. These are the plans which have been developed by people in the clinical community.

EXTERNAL FACTORS CAUSING CANCER

Mr. MICHEL. How do we really know that 90 percent of cancer cases are really external factors?

Dr. RAUSCHER. Migrant studies primarily. We know that the Japanese male living in Japan has the highest rate of stomach cancer of any group in the world and one of the lowest rates of colon cancer. When they move to our country, to Hawaii or to the mainland, within something like two generations their risk of stomach cancer falls—and ours is among the lowest in the world.

Mr. FLOOD. Would you yield? You mentioned the Japanese stomach cancer.

Because of the practices and customs of Japan the men sit down to eat first and the ladies serve the men. The men get the red hot food right out of the kitchen.

The ladies come in and sit down later on and the food in more ways than one is not so hot. Therefore QED the men have a high incidence of stomach cancer.

Dr. RAUSCHER. I have heard that many times. It is a possibility.

Mr. FLOOD. I sat there in Japan one day eating hot food and leaving a lady standing.

Dr. RAUSCHER. In any event, the reason we think it is up to 90 percent is that there is something happening in Japan putting that person at a high risk to one cancer and a lower risk in another. Moving to this country it flip-flops after he takes on our food habits, customs, and other sociological ways of living. It is not something inborn.

I could go through many others.

Mr. MICHEL. When you say 90 percent as a matter of fact and then cite one example I would not ask you to take up the time of the committee to cite many others.

Dr. RAUSCHER. There are many other examples.

CLINICAL EDUCATION PROGRAM

Mr. MICHEL. When you get to manpower and construction, you say a new cancer clinical education program will make awards to medical schools for the creation of innovative education programs. Who really determines what is an innovative education program?

Dr. RAUSCHER. These proposals will come from medical schools as to how they think they can best inform medical students, paramedical personnel, nursing, and so forth. They will propose their ideas to the NCI and we will try to pick the very best with advice from peer review groups.

Mr. MICHEL. You have a request for the National Institute of Education which has not exactly had very smooth sailing in this committee. Supposedly we are told these are the dreamers, and the chairman used the expression the head shrinkers, who will tell us how we do things more modernistically, new innovative means of educating. Will that institute have anything to do with determining what these innovative programs should be with respect to medical schools?

Dr. RAUSCHER. Probably not.

Mr. MICHEL. Why wouldn't they? Do medical schools have something different in the way of innovations than in the Office of Education?

Dr. STONE. We are talking about different levels of education. Medical school professional education is in many respects quite different from the problems addressed by the National Institute of Education. Medical schools, interestingly enough, have been in the forefront among institutions of higher education in establishing new approaches to medical education. On a number of campuses—Buffalo is an outstanding example, so also are the University of Illinois and Ohio State—there has been very fine collaboration between those members of the university departments of education who are interested in adult education and professional education and members of medical school faculties.

Mr. MICHEL. We have a new medical school in my home community. I was reading an extensive article in the paper and this has been bugging the dean because of the kinds of salaries being paid. He is rather reluctant to disclose them. They ultimately were disclosed. It is on a shared basis.

Some of the medical specialists in the community will be teaching part-time and practicing their profession at other times. This seems to be a very fine way of making the most of the resources we have in our community.

Dr. STONE. There is a natural alliance, which benefits both parties very much, between the medical school and the practicing community.

Mr. MICHEL. I am happy to have you draw the distinction between what special problems are involved here, higher education in medical schools and the other area.

COMPREHENSIVE CANCER CENTERS

What part of your budget goes for the comprehensive cancer centers. Would you show us, for the record, how funding for the centers has grown since their initiation?

To what extent was your institute involved financially in the Anderson, Sloan-Kettering and Roswell Park centers before the National Cancer Act, and how has your support to these grown since?

Dr. RAUSCHER. The concept of comprehensive cancer centers was put into operation during 1973. At that time three centers, M.D. Anderson Hospital and Tumor Institute, Memorial Sloan-Kettering Cancer Center, and Roswell Park Memorial Institute were recognized as comprehensive cancer centers. Since that time the NCI has recognized an additional nine institutions. In fiscal year 1973, comprehensive centers represented 7.0 percent ($29,622,000) of the total NCI budget. In fiscal year 1974 8.3 percent ($48,990,000) and fiscal year 1975 8.2 percent ($49,167,000) of the total budget estimate will be used to support comprehensive centers.

The original three comprehensive centers have been receiving support from the National Cancer Institute for a number of years. The support provided these centers is as follows:

[Amounts in millions]

	1971	1974	Percent increase
M. D. Anderson Hospital and Tumor Institute	$3.97	$6.39	61
Memorial Sloan-Kettering Cancer Center	5.00	9.90	98
Roswell Park Memorial Institute	2.93	6.88	135

DIFFERENCE BETWEEN A COMMUNITY CANCER CENTER AND A COMPREHENSIVE CANCER CENTER

Mr. MICHEL. For the record, how does a community cancer center differ from a comprehensive cancer center? What services does it provide? What part do you play in initiating community cancer centers? How are they funded, and how many more are you planning in what areas?

Dr. RAUSCHER. Comprehensive cancer centers are major multidisciplinary efforts, often associated with a university, with both research and clinical components and serving large populations. Generally, community cancer centers are developing in areas of modest population where a medical school does not exist. These centers are closely affiliated with a nearby comprehensive program. They represent a method of translating the most recent research findings into clinical practice. Such centers are usually largely clinical in their orientation and provide for a regular and extensive interchange of ideas, personnel, and cancer data with an established cancer center. Consequently, they will be able to bring to cancer patients, physicians, and paramedical personnel the benefits of the most recent advances in cancer research and treatment modalities.

Community cancer centers are encouraged to develop an affiliation with comprehensive centers as an integral part of the comprehensive centers' community outreach programs. Exploratory (planning) proposals are also accepted from those areas where the need exists and the desire to affiliate with a comprehensive center and to plan for an effective community center are evident.

Community cancer centers are eligible for grant and contract support for cancer detection, education, research, and development and exchange of information, but will also develop local sources of support for their programs and utilize normal sources of payment for patient care.

One community center is already funded and underway at the Mountain States Tumor Institute in Boise, Idaho. Two organizations—the Wilmington Medical Center in Delaware and the Luzerne County Medical Society in Wilkes-Barre, Pa.—are presently engaged in planning for such centers with NCI exploratory studies grant support. It is expected that as many as six to eight additional community cancer centers might be supported within the next year in various regions of the country. This is a new concept and the plans required to determine the number of centers to be established have not been completed.

ANTICANCER COMPOUNDS

Mr. Michel. In your discussion of treatment efforts, you say that more than 47,000 substances were screened for anticancer activity last year, and 15 compounds passed NCI's stringent tests in animals and were accepted for use in cancer patients. What kinds of cancer are these 15 compounds being used to treat? How effective are they, and how promising do they appear to be?

Dr. Rauscher. After evaluation in animal systems, the 15 compounds will be tested in man in what is known as a phase I study. In this type of a study, we attempt to determine the maximum tolerated dose and the type and severity of any toxicity. If toxicity is manageable and a tolerated dose can be determined, the drug will be tested in phase II studies for efficacy against several tumors with primary emphasis on the more common solid tumors—breast, lung, and colon. Even though all of these compounds have previously shown antitumor activity in animal systems, final evaluation of their potential in man will have to wait until the phase II studies are complete.

In the future, it is quite possible that the number of new drugs introduced into patients will be reduced. There are so many opportunities for reducing mortality through the improved usage of known drugs, that much of the clinical effort in the next years, will focus on currently available drugs.

FELLOWSHIPS AND TRAINING GRANTS

Mr. Michel. What will you be spending on fellowships and training grants compared with last year and the year before, and how many trainees are involved?

Dr. Rauscher. In fiscal year 1973, the NCI awarded $13,888,000 to fund fellowships and training grants, representing 1,115 individual trainees. With the released 1973 impounded funds, in fiscal year 1974 the NCI has $23,643,000 available, and it is estimated that this will fund 1,790 trainees. In fiscal year 1975, NCI estimates 1,378 trainees will be funded with $18,163,000.

Mr. Michel. How will the new cancer clinical education program work? Are these grants to schools?

Dr. Rauscher. The clinical education program is a new program initiated by the National Cancer Institute, which will be funded with grants. These grants will be awarded to schools of medicine, osteopathy, dentistry, and hospitals affiliated with schools of medicine.

The purpose is to encourage planning and development of educational programs aimed at achievement of optimal care for cancer patients, to enable students in the health professions to acquire basic knowledge, and to stimulate and expand efforts in cancer education.

EXTRAMURAL RESEARCH

Mr. Michel. Last year during the hearings, we discussed the portion of cancer research that is in-house and the portion that is extramural. At that time, you said about 10 percent was in-house. Is that still the case? Would you, for the record, provide us with a breakdown of who is doing the extramural work? That is, what percentage is through grants and what is through contracts? How much is done by private, for-profit organizations; how much by universities; and so forth?

Dr. Rauscher. In 1974, the Institute plans to obligate 7 percent of its available funds for intramural research and an additional 8 percent for NCI management and NIH Management Fund costs. Of our available funds in 1974, we also plan to obligate 36 percent for contracts and 49 percent for grant activities. It is further estimated that the Institute's extramural funds (from both grants and contracts) will be awarded in the following manner: 17 percent to profitmaking organizations, 52 percent to academic institutions, 24 percent to nonprofit organizations, 6 percent to Government agencies (Federal, State, and local), and 1 percent to foreign institutions.

LEUKEMIA

Mr. Michel. Last year in our discussion of leukemia, you mentioned that progress had been made with respect to the adequacy of care to children. As I recall, you said that at the beginning of the year you felt that only about 20 percent of our children really had access to the new technology that was just coming off the pipeline, and you thought that at the time of the hearings, that percentage had jumped to 50 percent. I was quite impressed with that rapid jump. How has that situation changed now?

Dr. Rauscher. Fifty percent would be a minimal figure. Over the past year, we have placed great emphasis on the transfer of research findings to medical practice. The cancer control program and the cancer centers have expanded greatly, to the point where the majority of our citizens have access to hospitals where they can receive the kind of specialized treatment that affords the best chance for cure. In establishing these centers, we are putting particular emphasis on their geographic location. We can expect that 50 percent figure to rise significantly during the coming year as these hospitals begin full operation in the area of acute lymphocytic leukemia.

GROWTH IN CANCER INSTITUTE BUDGET SINCE 1970

Mr. MICHEL. Dr. Rauscher, the budget for the National Cancer Institute has seen a phenomenal increase in the past 4 years. It was about $184 million, total, in fiscal 1970; then it jumped $40 million the following year, $150 million the next year, $112 million the next, and $45 million last year. Now, you want to go up another $70 million. According to my math, here, that's an increase of about 327 percent, isn't it?

Now, how in the world can one agency absorb all that money in such a short period of time? How can you expand your program to more than three times its size in less than 5 years? Doesn't that put a terrific strain on the administrative capability of the Institute? How have you been able to cope with this?

How much of an increase in administrative staff has there been during this period?

What kind of audit and review mechanism do you have to make sure these additional funds are being spent properly?

Dr. RAUSCHER. Based on obligations of $181 million for fiscal year 1970 and a request for $600 million for this year, the percentage of increase would be, I believe, a little over 230 percent.

As you noted, this represents a healthy growth; a growth which, however, has occurred over a 5-year period. The point I would like to establish in breaking out these increases on a year-to-year basis is that the substantial fund increase has not been awarded to the Institute in a single increment and thus has been appropriated in an orderly year-to-year manner. Even before the passage of the National Cancer Act of 1971, we have deliberately tried to plan program efforts beyond the level of currently available resources. Upon the advent of the national cancer program, we called upon many members of the scientific community who, through the medium of the national cancer strategic plan, continued to identify in terms of priority, impact, and feasibility key areas of cancer research. The scientific opportunities are present, and the required manpower and resources necessary to do the work are available in hospitals and clinics and in the laboratories of universities, medical schools, research centers, nonprofit and commercial organizations.

This growth in program has imposed a considerable strain on the administrative capabilities of the Institute. This has been relieved in part by addition of staff, which has increased from 1,355 in 1970 to a projected level of 1,855 in 1975.

Of the total number added to the NCI staff since 1970, approximately 210 are for administrative activities, primarily to support the expanding efforts in grant and contract activities.

The program and its program components are subject to continuous review at many levels. These include internal review within the NCI Divisions and by the Institute Director, review by external committees advising the Divisions and their program components; by the National Cancer Advisory Board and President's cancer panel, NIH, DHEW, OMB, and by the Congress. Scrutiny at all of these levels serves to provide maximum assurance that public funds are effectively spent.

ROLE OF A "LEAD" INSTITUTE

Mr. Michel. Dr. Rauscher, we are making a tremendous effort here, through the programs of your Institute, to stop a deadly killer of mankind—cancer. The Heart and Lung Institute is making a similar effort against disease of those organs, but in looking at their justification I noticed reference to a recent analysis of some 175 scientific discoveries that had to be made to permit the "great clinical advances of the fifties and sixties in the treatment of heart, blood vessel, lung and blood disease." This analysis showed that 36 percent of these discoveries were basic and completely unrelated to these diseases; 31 percent were made in basic research designed to contribute to solution of a clinical problem; and 33 percent were made as a result of applied mission-oriented research.

Now, that first percentage figure is one that gives me a little bit of trouble. Would it be true in the area of cancer as well as heart and lung, that a third or more of the work you build on would be the result of discoveries completely unrelated to cancer research? If this is true, doesn't it mean that the work of the other Institutes could be just as important to the battle against cancer as the work of the Cancer Institute? Aren't they all very much interrelated, and shouldn't we be concerned about focusing all our attention on one "lead" institute?

Dr. Rauscher. Rather than say that certain advances in cancer have been based on discoveries completely unrelated to cancer, I would suggest that such findings stem from work not directly focused on cancer, but found to have relevance to cancer as well as to other disease problems. Your point, however, is certainly a valid one and in terms of facilitating progress against cancer, provides a compelling justification for support of fundamental research not only by the NCI but also by the other Institutes whose disciplinary interests often complement or overlap those of NCI. Thus, we view the virology programs of NIAID and NINDS, the blood program of NHLI, the genetics program of NIGMS and the aging program of NICHD—to name only a few—as having great potential relevance to NCI objectives. I believe in similar fashion, that other institutes feel that a number of NCI-supported studies may yield information that will shed light on the categorical disease problems of greatest concern to them. Thus, since all diseases reflect a complex array of abnormalities of structure and function at subcellular, cellular, organ, organism and population levels, all Institutes have an inseparable community of scientific interests which, in respect to basic research, cannot in many cases be defined solely in terms of organization or categorical disease.

On the other hand, in my estimate when intensifying an attack on any particular disease entity, it is entirely fitting and necessary to emphasize the role and responsibility of the "lead" organization in achieving identified goals. Due to the sort of scientific interdependence you have mentioned, the "lead" organization clearly cannot thrive in isolation.

Yet, the "lead" organization must assume the responsibility of integrating the inputs of other organizations into the information and resource pool utilized by specific programs in striving to accomplish clearly identified, disease-oriented goals.

Mr. MICHEL. Dr. Rauscher, I think it would be good if you could spell out for the record what activities at the other National Institutes of Health are a part of the national cancer program, and which other Federal agencies are involved, and how they are involved. Would you do this please?

Dr. RAUSCHER. Yes, sir. I would be happy to.

The National Cancer Institute and the other NIH Institutes share a broad community of scientific interests, and all the other institutes conduct or support work either directly or tangentially related to the national cancer program. The cancer process represents abnormalities in the most fundamental life processes that are involved in the genesis of the full range of human diseases. Fundamental probes of the normal and abnormal biologic process are conducted and supported by all of the Institutes. In like fashion studies supported by NCI are likely to have great relevance to the disease-centered interests of the other Institutes. Following is a representative, but not exhaustive list of programs in other Institutes with direct relevance to cancer.

NHLI

Lipid metabolism (proposed role of fat in the causation of certain human cancers).

Lung diseases (lung cancer is responsible for the greatest number of cancer deaths).

Blood diseases (relationship of blood coagulation factors to cancer growth and spread).

NIAID

Transplantation and immunology (factors which relate broadly to the cause, prevention, diagnosis, and treatment of cancer).

Virology (impacts directly on one of the major factors involved in cancer causation).

NIAMDD

Nutrition (an area of increasing potential significance in respect to cancer causation).

Molecular biology (a basic field which is shedding light on mechanisms of cancer causation as well as approaches for cancer prevention, detection and treatment).

NICHD

Molecular genetics (a field which can provide insights concerning mechanisms of cancer induction, prognosis and response to treatment).

Aging (may provide information illuminating the role that the aging cell and organism may play in the outset, prevalence, and progress of the neoplastic process).

NIDR

Oral cancer (a subject of direct relevance to NCI interests).

NIEHS

(The interests of this Institute and NCI, particularly in terms of chemical carcinogenesis, broadly coincide).

NIGMS

Genetics (an extensive and broad-based program with great potential relevance to the factors underlying the initiation and expression of cancers).

Cellular and Molecular Bases of Disease.

Biomedical Engineering.

NINDS

Virology (viruses may play a part in a number of puzzling neurologic diseases. The nature of such "slow viruses", the mechanisms through which they may induce disease and their possible relation to cancer-causing viruses are being explored).

Brain tumors (an area of immediate relevance to NCI activities).

In addition to these programs in our sister institutes, there has been extensive coordination of Federal programs for a number of years. The National Cancer Act of 1971 has given impetus to the broadening of interagency cooperation and joint efforts, and there now are several major Federal program areas that the national cancer program has included in the combined Federal responsibilities. In some instances, these programs are most strongly related to existing executive departments such as the Department of Health, Education, and Welfare. In other instances, particularly the more intensive areas, the coordination liaison involves a discrete organizational unit within a department of Federal organization.

For example, the Food and Drug Administration and the National Institute for Environmental Health Sciences have funded programs emphasizing research concerned with cancer causation. FDA's work at the National Center for Toxicological Research and the Bureau of Biological Standards includes chemical and viral cancer causation and prevention activities. The Regional Medical Program Service has supported cancer control activities, and the National Institute for Mental Health has funded a few projects on drugs and psychological aspects of cancer. The National Institute for Occupational Safety and Health is pursuing research studies concerned with standards and control of carcinogens in the work environment.

Other involved agencies include the Departments of Transportation, Interior, and Labor which also have interests in various aspects of working conditions and environmental contents. The Department of Interior's effort, for example, has been concerned with the control of potential carcinogens affecting miners, and the Department of Labor's Occupational Safety and Health Administration has been concerned with enforcing standards for levels of carcinogenic material exposures to workers. The Environmental Protection Agency supports research related to controlling carcinogens in the general environment. The Atomic Energy Commission, because the relationships between cancer and radiation are so important, conducts a full spectrum of research and control activities concerned with all aspects of radiation and cancer. NASA and the Department of Transportation also have funded research on radiation.

Because of their responsibilities involving veterans, servicemen and their dependents, the Department of Defense and the Veterans' Administration conduct many research and control activities, including the cancer pathology effort of the Armed Forces Institute of Pathology. The National Science Foundation supports many fundamental research projects important indirectly for the advance of cancer research. Several programs in the Department of Agriculture significant for cancer include research on tobacco, tumors and tumor-bearing animals, virology, genetics, metabolism and nutrition. In addition, Agriculture has control programs for food, pesticides, and herbicides.

OCCUPATIONAL CANCER

Mr. Michel. Last year, an AFL–CIO witness (Jacob Claymen, administrative director of the industrial union department) testified about the lack of serious attention to occupational cancer. Could you supply for the record a list of research projects underway in this field with the amount of funds allocated to each? And would you tell us about the state of knowledge about this form of cancer, that is what we know and what we don't know.

Dr. Rauscher. I will provide that information for the record.

[The information follows:]

Occupational Cancer

Two large studies are underway on the development and detection of cancer in individuals who have had massive occupational exposure to carcinogenic materials. One group is comprised of uranium miners from the Colorado plateau, and the other consists of a number of workers from the Tyler, Tex., area who have had massive exposure to asbestos. These are population studies on groups at extremely high risk to the development of occupational cancers. The Colorado study has an annual funding level of $140,000 and the Tyler study has an annual funding level of $387,000.

Another major activity with the Stanford University, with an annual funding level of $650,000, is directed toward the gathering of information on the production, distribution and levels of human exposure for a variety of industrial and environmental chemicals. Substances brought to our attention through this program or other information gathering pathways are introduced into our bioassay program so that we may assess their carcinogenic effect in rodents. Contracts supporting studies on compounds considered to be occupational hazards include:

Contractor	Study title	Annua funding leve
Cincinnati, University of	Study of the carcinogenic and co-carcinogenic properties of industrial chemicals.	$94,828
Dow Chemical Co	Carcinogenesis bioassay of environmental chemicals	84,000
Georgia, Medical College of	Carcinogenesis bioassay of environmental chemicals	75,000
Hazleton Laboratories	Carcinogenesis bioassay of pesticides and other environmental chemicals.	480,000
Litton Bionetics	Carcinogenesis bioassay of environmental chemicals	600,000
Mason Research Institute	Carcinogenesis bioassay of environmental chemicals	631,315
Nebraska, University of	Carcinogenesis research and bioassays	1,000,000
San Francisco, University of	Studies of carcinogenicity of metallo-organic compounds	130,000
New York University Medical Center	Studies in pulminary carcinogenesis	387,000

LEUKEMIA

Mr. Robinson. As you probably know, I had a son who died from leukemia some years ago. He was 28. You mentioned the improvement in techniques, diagnosis, and treatment of leukemia in young patients.

I am naturally concerned about such treatment and the advances since that time regarding treatment of people his age. What has been the improvement and the advances which have been made?

Dr. Rauscher. They have been made but are not as dramatic as in the case of a child with leukemia. In using combination forms of drug treatment now, we have come much further than we were several years ago in knowing which drugs to put in combination. If we are talking about chronic monocytic leukemia, the survival rates have improved substantially. If we are talking about chronic lymphoid leukemia there has been less improvement involved. It is a harder cancer to control. Yes, improvements have been made but not nearly to the extent they have been made with childhood leukemia.

Mr. Robinson. At that point in time it was true, I believe, that a high proportion of those who did not survive, died not of leukemia but of complications associated with it.

Dr. Rauscher. That is right.

Mr. Robinson. Or from the adverse reactions to some of the treatments which were given. Is that still the case?

Dr. Rauscher. That is right. I think the predominant cause of the mortality is infection with rather common bacteria. The body's immune system is greatly depressed when you treat with anticancer drugs.

There have been substantial improvements in controlling this as well, using laminar-flow air rooms where there is a sweep of air from behind the patient into a collecting filter. This has greatly reduced the infection rate when the patient is undergoing extensive chemotherapy.

Development of newer antibiotics has helped. Specifically antibiotics against fungal infection has helped a great deal in cutting that kind of infection rate down.

The physician is getting a better way of controlling this disease.

CHEMOTHERAPY

Mr. Robinson. In terms of the chemotherapy, do you have drugs which you use today which do not have as much of the undesirable side effects as they did at that point?

Dr. Rauscher. We certainly do. It is drugs that have a lower toxicity or drugs which can be used at very high doses but the toxicity of which can be neutralized. One of the newest is the treatment of children with sarcoma with near lethal doses of methotrexate under ordinary circumstances. There is an antidote called citrovorium factor. If you administer that to the patient at a certain time after this high dose, it neutralizes the toxicity, even to the point of a child not losing hair or experiencing other common symptoms of toxicity. That is the kind of thing we are using for controlling the toxicity while at the same time taking best advantage of the anticancer effects of the drugs.

LUNG CANCER

Mr. Robinson. On another subject with regard to the use of tobacco. we know that the incidence of carcinoma of the lung in males is so much higher than it is in females. Do we know any more about why that is now than we did a year ago?

Dr. Rauscher. Women are beginning to smoke much more than they used to. As a matter of fact, you can pretty much pinpoint the time where tobacco consumption among women——

Mr. Flood. You say they are beginning to?

Dr. Rauscher. Beginning to smoke far more than they used to. You can almost pinpoint the time when tobacco consumption among the female population began to increase and some years later you can see their risk to lung cancer increase as well. Probably this is the same reason for an increase in esophageal cancer and lung cancer among black men and women. As our society becomes more affluent you begin to drink more and smoke more and do the things we know we should not do. This places us at some increased risk to these cancers.

Mr. Robinson. So the incidence of lung cancer among females is increasing?

Dr. Rauscher. It is in fact increasing, yes.

Mr. Robinson. To what extent?

Dr. Rauscher. I think I am right in this—that lung cancer in the female, the white female, is increasing more rapidly than cancer for any other site in the female. I can get you better data, showing whether it is doubling or quadrupling but I cannot be that accurate right now.

Mr. Robinson. I would like to have that information submitted at this point, Mr. Chairman.

Mr. Flood. Very well.

[The information requested follows:]

RATE OF INCREASE OF LUNG CANCER IN FEMALES

Within the United States, for both men and women, mortality rates have risen faster for non-whites than for whites (Fig. 1). For women of both races, the rates have increased more rapidly than for men, particularly in the last decade. This more rapid increase in women can also be seen by looking at the ratio of male-to-female deaths (Fig. 2). For whites, the male-to-female ratio reached a high of about 6.8:1 in 1960, and has been declining ever since. This is not because male deaths have declined, but because female deaths have risen more rapidly. For non-whites, it is not clear whether a peak has been reached yet. The data suggest a peak, perhaps 3–4 years later than the peak in whites, and a slower decline (if any) than among whites. In any event, the women's rates, while still substantially lower, are approaching the rates for men.

Figure 3 demonstrates cigarette smoking data for women. Among women, of the same attained age, the movement from one cohort to the next is opposite from what one sees among men. Among women, the movement is *upward*. For the cancer ages (45 and above), each succeeding cohort of women has had more smokers than the preceding cohort. (There is one exception; in the 1970 survey, 1% fewer women between the ages 45–54 were recorded as "current cigarette smokers" than in the earlier survey.) Thus, for women, we do not anticipate any decline in the mortality rates from lung cancer in the near future. We should expect more women to develop lung cancer and subsequently to die from it. The male/female ratio which has started to decline should continue to decline.

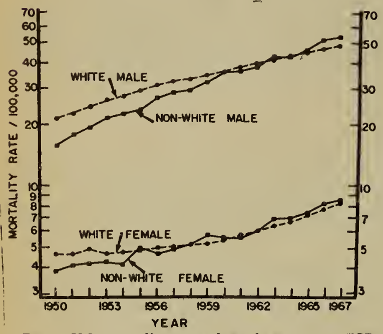

FIG. 1. U.S. mortality rates from lung cancer (ICD 162 and 163), age-adjusted to 1960.

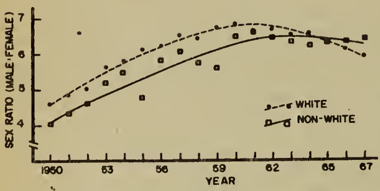

FIG. 2. Sex ratio of mortality rates from lung cancer (ICD 162 and 163) for United States.

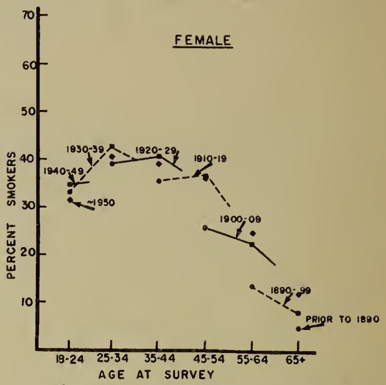

FIG. 3. Trends in smoking for U.S. women. Percentage of smokers reported as "currently smoking cigarettes" on surveys taken in 1955 (●), 1966 (■), and 1970 (◆), plotted by age at survey and year of birth cohorts.

Excerpt from Schneiderman,M.A. and Levine, D.L.
Trends in Lung Cancer.
Cancer 30: 1320-1325, November 1972.

Incidence: Third National Cancer Survey, 1969-1971. Incidence rate/100,000 for cancer of the lung and bronchus, age-adjusted to 1970.

	White	Black
Male	70.6	89.6
Female	14.4	14.4
Male:Female ratio	4.9:1	6.2:1

Mortality: National Center for Health Statistics, 1970. Mortality rate/100,000 for ICD 162-163 combined (lung, etc.)

	White	non-White
Male	55.2	44.7
Female	12.5	9.0
Male:Female ratio	4.4	5.0

SUMMARY:

The trend in lung cancer among women shows rising incidence and mortality. This is believed to be due primarily to the increase of smoking among women. There is no evidence to indicate that these trends will change; we expect lung cancer rates among women to continue to rise.

EDUCATING THE PUBLIC ON THE EFFECTS OF SMOKING

Mr. Robinson. How much is the National Cancer Institute spending with respect to trying to educate the people regarding the dangers of the use of tobacco?

Dr. Rauscher. Our total program in tobacco research and antismoking in 1975 will be about $8 million. It is $7½ million in 1974. Some of this is through the National Clearinghouse for Smoking and Health under the direction of Dr. Horne. Other projects are designed to evaluate the carcinogenicity of tobacco products. Part of the overall effort is to try to work with industry to develop a less hazardous cigarette by reducing tar.

Mr. Robinson. How would you evaluate the cooperative attitude of the tobacco industry with respect to this research?

Dr. Rauscher. I know that they are interested in developing cigarettes with lower components of those chemicals which in animals are known to cause cancer. They are supporting research to some extent in this area. I think much more needs to be done.

We do have a Government-industry work group in tobacco carcinogenesis where my people and the people in other academic institutions in the country meet together with people from industry to try to plot the strategy as how best to do what has to be done. It is developing.

COMPETING AND NONCOMPETING GRANTS

Mr. Robinson. Turning again to the figures shown on page 23 of your justification which were brought to our attention by the chairman, it is very apparent that the real increase in the amount of money in grants in your first section there is in noncompeting grants. In competing grants it is true that you are increasing the number from 473 to 533, but even if you add the additional money, up to 589 from 530 shown at the bottom line, it certainly constitutes a substantial decrease in the amount per grant in the competing area whereas your increase is in the noncompeting area.

Dr. Rauscher. That is right.

Mr. Robinson. What is the rationale for going further in the noncompeting grants and cutting back on the competing ones which, it would seem to me, would provide you with what competition always provides in terms of additional value for your money?

Dr. Rauscher. This is a basic phenomenon of using the grant mechanism. When you have a very good funding year, like a year ago or two years ago when our funds went up quite substantially, you are able to award many more competing grants than you ordinarily would. Our best year was in 1972 when we were funding something like 65 percent of approved grant applications.

When you do that, however, you essentially lock yourselves in for a 3- to 4-year funding period. We provide a moral commitment to an approved grantee when his grant is paid for the first year, that we will, in fact, pay him for the second, third, and in some cases fourth year. That money is, therefore, not available to fund new competing or competing renewal grants.

About the only way you can fund continually an adequate number of new applications is with new increases from the Congress, and the OMB. If you don't get that, the percentage of payability for new grants drops off substantially.

Mr. Robinson. Does this infer, then, that a substantial portion of what is listed as noncompeting grants are actually continuations of existing programs?

Dr. Rauscher. Every one.

Mr. Robinson. All of them are?

Dr. Rauscher. That is right.

Mr. Robinson. What proportion of them might have been competing grants at their outset?

Dr. Rauscher. All were competing at the outset, either applications which the investigator initiates and comes to us for study section review and possible funding or——

ANNUAL REVIEW OF GRANTS

Mr. Robinson. To what extent are these grants for which you have moral commitments to continue reviewed on an annual basis?

Dr. Rauscher. The investigator submits a progress report. This is reviewed by in-house staff. The real major review comes after the 3 or 4 years, depending on the renewal of grant commitment. Then he actually has to reapply and he competes on an equal basis with other people who never have had a grant or who are also competing for the first time.

RESEARCH AND DEVELOPMENT CONTRACTS

Mr. Robinson. Almost a third of your budget of $600 million is in the area of research and development contracts. Are those competing to any extent?

Dr. Rauscher. Each contract must either be competed or, in strict accordance with Department of Health, Education, and Welfare procurement regulations, a complete written justification for noncompetition must be prepared and approved by senior NCI and NIH officials. In fiscal year 1973 approximately 60 percent of our new contracts were awarded on a competitive basis. The remainder were fully justified and approved as bona fide sole-source situations.

COMPREHENSIVE CANCER CENTERS

Mr. Robinson. With regard to the comprehensive cancer centers, to what extent are they outpatient facilities and to what extent do they have facilities for in-patient care?

Dr. Rauscher. Funds provided through the comprehensive center program can be used for patient beds but they must be cancer research beds and not general care or health delivery kinds of beds. Funds can also be used for outpatient care provided the research studies are done on cooperative clinical protocols. It has to be a research project and not just paying for a cancer patient as he comes in off the street.

Mr. Robinson. Do you have a figure as to the number of beds which are so available?

Dr. Rauscher. We have number of patients, I believe. In 1974 the number will be 78,000 in the country, which includes inpatients as well as outpatients. Through the national program a total of 102,000 patients will be studied and treated through funds from this program in 1974.

Mr. Robinson. I know these patients come in and are hospitalized a short time, go home, come back, go home again, and so forth. You have no specific figure as to the number of beds which you actually keep available for this purpose?

Dr. RAUSCHER. I have 198 beds at the Bethesda Center and nearby facilities. I can submit this for you.

[The information requested follows:]

Number of beds in cancer research centers

NIH Clinical Center	128
Veterans' Administration	30
Baltimore Cancer Research Center	40
Subtotal	198
Cancer research centers	2, 500
Total	2, 698

The estimated number of 2,500 beds in cancer research centers (both comprehensive and specialized) throughout the country is available for research, however many of these are utilized for patient care where research is not involved. In those cases. funding is not provided through the National Cancer Institute.

Mr. ROBINSON. Are all these comprehensive cancer centers located within the structure of an existing facility? None of these are brand new?

Dr. RAUSCHER. That is correct.

Mr. ROBINSON. They are all part of a functioning facility which does other things besides this kind of work?

Dr. RAUSCHER. That is right.

RECRUITMENT OF SCIENTISTS

Mr. ROBINSON. You mentioned with respect to recruiting personnel that you are becoming noncompetitive. What is your competition and in what areas are you noncompetitive?

Dr. RAUSCHER. It depends on the qualifications of the investigator or the clinician, the kind of person we need, and the level. If we are recruiting for levels at the very top of the pay scale we find we are able to offer less remuneration than many of the cooperative clinical centers or cancer centers in the country. As we develop more and more facilities such as comprehensive cancer centers, the competition for the available manpower of most excellence becomes keener.

At the NIH, for instance, we no longer have a physician draft. This is one thing which perhaps may contribute to our being unable to attract the number of younger physicians that we need. Many factors go into this. The research and clinical opportunities at the National Institutes of Health are about as good as they are at any place in the country. It is because of this that we do continue to get an inflow of people at the younger age levels. However, when you try to go after a major person to head up an institute or head up a division within an institute, and these are very difficult jobs, it becomes more and more difficult to recruit them. I think this is primarily because of workload, because of salary constraints, additional benefit constraints, and so forth.

Mr. ROBINSON. You mentioned the competition of cooperative cancer research centers.

Dr. RAUSCHER. Yes.

Mr. ROBINSON. How many of those are there?

Dr. RAUSCHER. Well over 300 in connection with cancer clinical cooperative groups. These are people who use a common protocol to study drugs in a large number of patients in order to get information as quickly as possible.

CANCER CONTROL

Mr. ROBINSON. You mentioned the fact that one of your major areas of emphasis will be that of cancer control and that your budget is up $10 million. How is this information which you attempt to disseminate through the use of this money gotten out to more people?

Dr. RAUSCHER. There are quite a few examples I can give you. There will be 18 comprehensive centers. Each of these is responsible for coordinating activities within its immediate geographic area, so another 20 to 50 different hospitals and clinical groups can be cooperating with one of the cancer centers. It is up to the center director and his staff to get research information by way of visits, dial access, publications, and so on to get information out to the people within his area.

At the M. D. Anderson Hospital in Houston, for example, they have a dial access system where physicians in 28 States can call in and get information on over 200 different topics regarding cancer—what is the latest and best method of treatment for this particular kind of cancer? This is followed up within 2 days, usually 48 hours, with a computerized printout, further advising the physician as to what might be best for that particular patient, and advising him, also, that the treatment of the disease may be so complex that it might be better for the patient to be admitted into a major comprehensive center. This is the kind of thing we are doing now.

COMPREHENSIVE CANCER CENTER

Mr. ROBINSON. Is this particular comprehensive center the only one which is so equipped at the moment?

Dr. RAUSCHER. No. We have developing projects in Colorado and with the Fred Hutchinson Center as another example in the Northwest. They are in turn developing information-handling systems for community hospital physicians, as well as physicians who have better access to this kind of information in major clinical centers. We are not doing nearly as well as we must in getting the information to the family physician regarding best form of early diagnosis and whether to treat or not to treat. It is especially important when you remember that 80 percent of cancer patients are seen first by the practicing community physician.

It is terribly important to do this——

Mr. ROBINSON. I was thinking of a situation which I faced as a friend of the family recently when a young teenager began to deteriorate. Diagnosis was most difficult at the local level.

Dr. RAUSCHER. That is right.

Mr. ROBINSON. He finally wound up at Bethesda. The initial diagnosis took an inordinately long period of time. Do you feel this information, the fact that this information is available, is well enough publicized?

Dr. RAUSCHER. It is not well enough publicized. That is why we are developing these kinds of physician contact programs. It is not done as well as it should be. We are spending a lot of time, a major part of our resources, in trying to get this information out to the physician as quickly as possible. These poor fellows have all kinds of things to read and they haven't the time to constantly inform themselves as to what is the latest in cancer, rheumatoid arthritis, and other diseases. We have to do better, and I think we will.

Mr. ROBINSON. Thank you, Doctor.

Mr. FLOOD. We will resume at 2 o'clock

Mr. PATTEN. The committee will come to order.

Doctor, it is a pleasure to have you before our committee. I should tell the members of the commitee and your cohorts we know you up in New Brunswick and we are positive you are eminently qualified for the work you are doing. You have devoted so much of your life to it.

Mr. Chairman, I was just saying Dr. Rauscher was up at Rutgers 8 or 10 years, the best years of his life. He has earned an excellent reputation. In fact he received an award I hold very high, the Waksman Award, and he received many other awards.

We wish you the best of luck with the tremendous undertaking you have in this large budget. May God be with you in your decisions that you have to make.

I will yield to Mr. Obey.

LUNG CANCER

Mr. OBEY. Doctor, this morning in answer to the chairman's question as to whether or not you still felt cigarette smoking was the main cause of lung cancer you said "yes" and pretty much let it go at that if I recall correctly. I am a nonsmoker. I used to smoke three packs a day but I quit. But I recall the chairman asking you last year what the causes were of increases in lung cancer and at that time you responded as follows:

> There are a number of things that appear to be associated with an increase in lung cancer. Pollution of the environment is known to be a contributing factor. If one lives in a highly industrialized city the risk of lung cancer is greater than if we live on the plains of Iowa.

You went on to mention tobacco, that there may be genetic predisposition.

You later made the statement that 80 to 85 percent extrinsically acquired disease.

Then in answer to a question by the chairman, "Are you making any strides in improving the chance of the survivor victims of lung cancer," you said, "Yes." You mentioned techniques to be used such as getting people to live in cleaner environments, use tobacco less, and to protect workers in shipyards, things like that.

Let me ask you this:

As I understand it each year we propel about 200 million tons of toxic substances into our air and 60 percent of that I am told comes from the internal combustion engine.

Let me ask this: Has your agency done thinking at all about the cost in terms of additional cancer which would be associated with the President's recommendations on loosening the clean air standards announced day before yesterday?

Dr. RAUSCHER. We have, Mr. Congressman, made estimates as to the cost of cancer in this country. This combined with our strong belief that 85 percent of man's cancers are extrinsic in nature, and that the most prevalent form of cancer is lung cancer is of course great cause for concern.

In terms, however, of specifically reducing the requirements for auto emissions, we have not done any specific thinking on that except to know very clearly that increased emissions will increase contamination of the environment and possibly increase one's risk.

There are so many cost-benefit factors that go into the identification of carcinogens and the prevention of cancer that it is almost impossible to say this must not be done because this is what will happen. As you very well know, if it is in some cases not done, other things will happen that will be deleterious to people as well.

My job is to do whatever I can to encourage people and agencies to reduce the carcinogenic burden in the environment, and this is one of our major thrusts.

AIR POLLUTION

Mr. Obey. I understand it has been estimated by some that a 50-percent cut in air pollution would reduce lung cancer mortality by about 25 percent. Is there any accuracy to that assertion or not?

Dr. Rauscher. It is probably in the ballpark. You know if we could do away with cigarette smoking we would reduce it probably by 85 percent.

Mr. Obey. There were three items I worry about in the administration package. No. 1 is broadly allowing the use of more coal. Second, the delay in the auto emission standards schedule, and third, the delay in requiring your large cities to meet the clean air standards.

The net effect of one provision in the administration bill, as I understand it, would mean that major urban centers could have as much as 15 years to meet the minimum clean air quality standards of the 1970 act.

If you haven't done any computation in your shop at all on the auto emission delay, is there any way you can compute, based upon past estimates in either your shop or someplace else, what the increased number of cases of cancer would be in, say, a city like Los Angeles over a 13-year period?

Dr. Rauscher. I think there are probably ways of coming up with a better judgment than a guess I could give you right now. We are in fact doing quantitative studies in Los Angeles and other cities in the country.

Mr. Obey. I would appreciate it if you could put something like that in the record. I would be interested in knowing what it would be. Take any five major cities in the country you want. And, if you would, also apply it nationally. We are getting a lot of discussion about the benefit in terms of the easing of the clean air standards, not an awful lot of discussion about what the cost will be.

Dr. Rauscher. We will try to do whatever we can on this. It is a very complex kind of thing because you are dealing with people of different genetic backgrounds, of different ages and so forth.

In lung cancer there is another complicating factor. That is we know if a person who has been smoking for let's say 20 years gives up the habit his risk of developing lung cancer would in a few short years revert almost back to normal. Unlike many other cancers it is not essentially a cumulative kind of phenomenon. You do revert back to normal.

Let's say pollution increases over the next 5 to 6 years because of some of the things you are talking about. If in fact they are cleaned up after that time and because the latent period to exposure and development of cancer is so long, that impact of contaminated environment is almost not measurable.

[The information follows:]

CLEAN AIR QUALITY STANDARDS

Although there is not any direct evidence on the effect of air pollution in general or of automobile emissions in particular on the incidence of cancer, comparison of cancer incidence in urban and rural areas indicates a higher incidence of cancer of the lung. A variety of factors have been implicated in the observed difference, including specific industrial exposures, cigarette smoking, as well as air pollution.

Proof is nonexistent to date that any specific air pollutant causes tumors in man. Not even the concentration and physical state of damaging elements at the human receptor site—that is, distal pulmonary parenchyma—have been adequately established. Available evidence suggests the interaction of two or more elements through synergistic or cocarcinogenic mechanisms. Although available knowledge does not permit quantitative estimates, evidence at hand points to a relationship between air pollution and the incidence of lung cancer. The benefit of reducing pollutants in the air can be inferred from animal experiments with cigarette smoke. In an experiment by Auerbach and Hammond, beagle dogs smoking filtered cigarettes developed fewer lung tumors than beagles smoking unfiltered cigarettes. Cigarette smoke and automobile emissions both contain high-concentrations of polycyclic aromatic hydrocarbons, which have been shown to be carcinogenic in animal experiments. Thus, in qualitative terms it is reasonable to assume that easing of automobile emission standards will delay the potential reduction of lung cancer incidence expected to result from cleaner air.

Mr. OBEY. Let me quote you last year's hearings. I said this:

> You said if we could apply existing information as much as we would like, we could probably reduce lung cancer deaths by one-third. Could you give me some examples of the things that you would like that are not being done?

You answered:

> We know of three specific factors related to an increasing risk to lung cancer. No. 1 is exposure to asbestos; No. 2 is environmental pollution; that is, comparing rates between the city and farm dwellers; and third is exposure to tobacco and tobacco products.

Mr. Flood mentioned textile mill plants. You said, "Any small particles that hang around for a long time are suspect."

Then you went on to say, "There may be ways of inducing our enzymes or our body chemistry to ward off the toxic effects of what you are being exposed to." Then you say:

> What I am saying is, if we could decrease the exposure to asbestos and environmental pollutants, and most important, decrease our intake of or modify our response to noxious chemicals, at least a third reduction in a few short years would be realized.

If you mention the third last year, I would think you would be talking about a substantial amount. I recognize all the variables, but I think nevertheless that a judgment could be made. I would hope a judgment could be made by yourself.

Dr. RAUSCHER. I think so, yes, and I stand by that statement.

Mr. OBEY. Do you want to add something, Dr. Stone?

Dr. STONE. I wanted to point out that the National Institute of Environmenntal Health Science, headed by Dr. Rall, is presently engaged in developing a plan for examining the consequences of new methods of energy production wholly different from those that we are presently using. We think that the health consequences might be quite substantial. When Dr. Rall is here, I know he would be available to discuss that with you. We think that it is something worthy of a great deal of our attention now.

Furthermore, smoking and air pollution also affect the lung in ways other than cancer, and when Dr. Cooper talks this afternoon he might have some information on that topic.

We are trying to look at changes in our environment and lifestyle in a wholistic way and to look, particularly, for synergistic effects.

The effects of chemicals are sometimes more than additive. That is, when you are exposed to a certain amount of one chemical and a certain amount of another chemical, the result is frequently not a simple 1 and 1 makes 2; the result is frequently 3 or 5 or 10, in terms of the delerious effects this dual exposure may have on the body.

ENVIRONMENTAL HAZARDS IN THE WORKPLACE

Mr. Obey. That brings me to some of my other questions.

Dr. Rauscher, in your statement, you said this morning: "New projects planned for 1975 include efforts in the control of the environmental hazards particularly in the workplace."

I wondered if you could expand on that a little bit and tell us a little more about it.

Also, can you explain to me how you relate to the Environmental Institute, how you relate to NIOSH? Mr. Flood was discussing this morning with you the different cancer rates of stomach and colon between Japanese and American citizens. How in fact do you take an issue like that and split it up between your shop and the Environmental Institute and NIOSH? How do you divide the responsibility?

Dr. Rauscher. We are working, Mr. Congressman, with at least 12 other agencies either to provide support for activities that they are set up to do better or more quickly than we can.

Secondly, in terms of providing consultation and information, a major source of cancer incidence information in this country concerning cancer rates, together with exposure of workers to various occupational hazards, comes from what we call our third national survey wherein we took 10 geographic areas in the country and determined what the cancer rate and incidences were. This information is applied on nearly a weekly, if not more frequent, basis to these other agencies.

The kind of chemicals—to get to the first part of your question, the kind of compounds we already know to cause cancer are such things as asbetstos and probably other small particulates equivalent to asbestos. It was due to the recommendations based on this kind of information from the National Cancer Institute that protective headgear and masks were introduced.

We work constantly with the Food and Drug Administration on such things again as asbestos, vinyl chloride, diethylstilbestrol which used to be a food additive for cattle. Again based in part on our surveillance and testimony, the Food and Drug Administration did take action to modify this exposure or eliminate the compound entirely from the environment. So there is a very, very close relationship to regulatory agencies. We do not have a regulatory mandate as you know.

HIGH FAT DIETS

Mr. Obey. My point is, if you take a specific question such as you had in the Post this morning, where you had discussion of the high fat diets and the probability of that leading to certain kinds of cancer, how in fact does the National Institutes of Health decide. I would like you to give me some examples of how specifically you split up your responsibility with the other institutes for instance.

Dr. Rauscher. First of all, when an observation like this comes along and this is now the second time——

Mr. Obey. Are you working on it at both ends?

Dr. Rauscher. Yes; the observation you are talking about is that a high fat intake, related specifically to a diet with a high beef content, may predispose one to a higher risk to colon cancer. Dr. Wynder, whose article you are speaking of, feels that other cancers like esophageal or rectal, may also bear this relationship to a high meat intake.

Again the data that he is basing his observation on comes primarily from the migrant study dealing specifically with the Japanese. These have yet to be confirmed. When anything of this importance comes up the very first thing is to confirm this in other population groups. This shouldn't take too long. We can do it retrospectively with existing medical records.

The next thing to do is try to determine whether, in fact, meat or meat protein or components thereof have a carcinogenic effect in an animal model system. All of the chemicals known to cause cancer directly in man are highly carcinogenic in animal systems.

I think before the National Cancer Institute would propose any overall recommendations for regulation for dietary modification we would want to make sure this observation is real.

I think we are another several years away from that kind of thing. In the meantime what we will do is continue to identify and follow high risk populations.

COOPERATION WITH OTHER NATIONAL INSTITUTES OF HEALTH

Mr. Obey. But that is not my question. My question is, How does the National Institutes of Health determine whether you go at that problem or whether the Environmental Institute goes at that problem? How do you decide who does the work on it?

Dr. Stone. May I reply to that, please? That is a specific responsibility of the Deputy Director for Science, Dr. Stetten. Dr. Stetten can explain the ways in which he is doing this.

In general, he looks at the specific legislative charges to the various Institutes as one way of deciding. Where it is written into the law that an Institute has a responsibility in a particular area, that Institute is very likely to be made what we call the lead agency. It is then the responsibility of the Director of that particular Institute to pull together a committee that includes individuals from other Institutes whose interests are perhaps somewhat less than that of the lead agency and to sort out, in discussion around the table, where particular responsibilities will be.

Biomedical science, as I think you imply in your question, has very many overlapping areas; the more fundamental the work, the more the difficulty in deciding what particular area the investigation or study relates to. For projects that are much more nearly applied research, the Institute relationship is perhaps more directly apparent.

I might suggest that perhaps Dr. Stetten could add further to this from the standpoint of coordination of the scientific effort. It is something we try to facilitate, but we don't impose decisions.

Dr. STETTEN. Perhaps an example will suffice. There is a disease familiar to both Dr. Rauscher and myself, xeroderma pigmentosis. It is a genetic disease and, as such, falls in some degree in the Institute with which I was formerly associated, the Institute of General Medical Sciences, which had an assignment from the Congress to investigate and support research in genetic diseases.

In this disease the individual is extremely sensitive to sunburn, and it turned out that the genetic defect in this disease was an inability, due to lack of a requisite enzyme, to reconstruct damaged nucleic acid when it was injured by sunlight. When the nucleic acids of the skin are irritated or damaged in certain quite specific chemical ways, the normal individual, such as you or I, continuously repair the damage and we have the machinery to do it.

This machinery is lacking in certain individuals. The damage persists and the individual not infrequently develops skin cancer, presumably at the site of these damaged nucleic acids and as a consequence of this damage.

Work on this problem, which had much support in its early stages from the Institute of General Medical Sciences, is now, appropriately I think, in the domain of the National Cancer Institute.

This kind of movement of problems from one Institute to another is not the exception. It is part of the normal course of events and happens quite easily.

Mr. OBEY. I am asking a very specific question though. I am saying in the case of this thing discussed this morning, which institute will be the lead institute. Would it be yours or Environmental or would it be somebody else?

Dr. RAUSCHER. I think at the present time because of its implication for cancer, and so far only to cancer, we would certainly be the lead institute in this. But we work together.

As an example Dr. Rall, head of the Environmental Institute, was at our Board meeting for 4 days last week at which this very kind of thing was discussed as to what he can do and what we can do.

OCCUPATIONAL HEALTH

Mr. OBEY. What about occupational health? Some people complain to me there is in fact no identifiable occupational cancer program within your Institute. I know you are conducting research on it. I have had some people suggest to me there is not a specifically defined program as such in your Institute and there ought to be. What is your judgment on that?

Dr. RAUSCHER. We have a major program in trying to identify carcinogens and then recommend procedures for protecting the workers. It is our carcinogenesis program. There is about $34 million a year in the budget for this program.

In addition to that, once we do identify these things and show a protective measure can work, this then becomes the purview of our cancer control program, and there your people are correct. We have had no program prior to 2 years ago in which the fruits of this research were actually applied to demonstration projects by NCI.

We never had that mandate before, but we do now. A total of about $45 million in 1975 is what we are proposing to spend in cancer control. About $22.5 million will be spent in these kinds of preventive things for occupational risk and occupational exposures.

Mr. OBEY. That was last year. How much this year?

Dr. RAUSCHER. It has been about $2.5 million this year for the control activity. For the research activity it is of the order of $20 million.

Mr. OBEY. I am confused. You said it is $2.5 million this year and $4.5 million last year.

Dr. RAUSCHER. It is $2.5 million this year in the control demonstration kind of activities.

Mr. OBEY. How much was that last year?

Dr. RAUSCHER. Last year it was of the order of $2 million.

Mr. OBEY. So it goes up half a million?

Dr. RAUSCHER. That is right.

GENERAL BIOMEDICAL RESEARCH

Mr. OBEY. There are a lot of questions I could ask you, but I don't want to take much more time.

We talked about this with Dr. Stone yesterday. I am frankly a little ill at ease by the amount of money your Institute is getting in relationship to some of the other Institutes at NIH. At a party last night I was talking to five or six people, and three people who are familiar with the problem all voiced the feeling that a much better way to attack cancer is through the general biomedical route, rather than a specific attack on cancer. I would like to have your response to that.

Dr. RAUSCHER. I believe the best way to do this by far is to attack single diseases when the information base is appropriately large enough to attack a single disease. I think at the level we are spending in cancer now we have that kind of information base.

I would say also, however, that I completely agree that many leads that we already have, have come from investigators in other institutes or investigators in the rest of the country supported by these institutes. No question about that.

But I think another point that must be made is that progress against many other diseases will certainly come by investigators specifically performing so-called cancer work. It is a two-way street. This is why I continue to think the best place for the Cancer Institute and cancer people doing that kind of work is within the environment we have right now at NIH. We work as a team.

When a body of information becomes ripe enough to begin doing something in a targeted sense about specific cancers I think we have no choice but to do it. And cancer is so pervasive and so numerous that the funds we are spending in the targeted categorical disease are totally justifiable.

Mr. OBEY. Even at the expense of some of the other programs?

Dr. RAUSCHER. Certainly not.

Mr. OBEY. That is really what this budget has done. I would like to see everybody get more, but with the deficit situation where they can't, is this really the best balance? I know you are a hell of a guy to ask this of.

Dr. RAUSCHER. I have heard this argument many times. You can argue on both sides of the coin. They argue cancer funds are increasing at the expense of the other institutes. I sincerely and seriously hope this is not true.

I have been a great supporter and the people who advise me—Mr. Schmidt, chairman of the President's Cancer Panel, has continuously made the point that a healthy cancer program needs healthy other components of biological and biomedical research.

FUNDS FOR OTHER N.I.H. INSTITUTES

Mr. OBEY. What you are saying is the money you are getting you can certainly use, and if there are other problems in other institutes, they have to be attacked by this committee by raising the budget over the total amount and not by cutting back on your Institute?

Dr. RAUSCHER. I think again, as I mentioned before, the advice I am getting from cancer experts indicates we can spend the money we have very well and could spend more money just as well. I know the advice other people are getting from other components of the scientific community is such that additional funds could be spent very well.

Mr. OBEY. How do you define that? I would like to put a dollar figure on how much you could use. I don't know that we could fund it. Some people say that the National Cancer Institute can't now use productively everything you can get. You obviously disagree with that. Others say more could be used. How far do you go in any fiscal year before you reach the point beyond which the money could not effectively be used?

Dr. RAUSCHER. We have what is called a National Cancer Plan, a feature of which is to provide to the Department and the White House and the Congress each year a 5-year plan. I have had at least 250 of the best people in the country contribute to this plan. They have developed not only what the science base is and what science could be done but the cost of this in dollars, manpower, space. Over the next 5 years we have developed a high range, a midrange, and low range.

The advice that I have gotten, and that has been a recommendation made by the National Cancer Advisory Board, is that in 1975 funds up to $750 million could be spent very well. Now this is the high range.

I have always viewed as part of my job, in being responsive to this advice, to bring it to groups such as this, recognizing also that there are so many other compelling demands on the Federal dollars we probably will not attain the level proposed.

To answer your question specifically, that is the amount we think can be used very well. When you consider that for the first time, really the second time—but for the first time in the recent history of the National Cancer Institute we now have a mandate not only to support the best in research but to deliver that research in a demonstration sense to people and physicians throughout the country, and that is very expensive work. So we are not only talking about research, we are talking about applying research benefits to you and to me, to all people.

CANCER CENTERS

Mr. OBEY. Under the cancer plan how many years did you say it would take before you had 175 million Americans living within 60 miles of a center?

Dr. RAUSCHER. If we go to 32 centers as being recommended, that will cover at today's population base about 175 million Americans. They will be within those geographic areas.

It does not mean, incidentally, that they will all be treated there. But they are coverable. My guesstimate is it will take as long as 10 years because some of the specialized centers are just beginning to develop thoughts of attaining comprehensive status. In the meantime, however, if we can go to 18 or 20, a network of community hospitals can be set up all over the country, a network in which they plug in informationwise, competencewise to the centers that already exist.

In some cases I think realistically this is a very long distance. So we would prefer to see other centers on their own strive to attain comprehensive status so that all parts of the country will have near immediate access to that kind of competence.

UTILIZATION OF ADDITIONAL FUNDS

Mr. OBEY. If your Institute got $50 million more, what would your priority items be?

Dr. RAUSCHER. In terms of mechanism of funding we would put approximately 65 to 70 percent within the grants program including regular research grants, investigator-initiated applications, but also into centers.

Mr. OBEY. How much into centers?

Dr. RAUSCHER. If we had another 10 centers, we estimate that the core support per center would be of the order of $1 million the first several years. The rest of the money going into the centers would be through the regular competitive grant and competitive contract mechanism. So next year, if we can strive towards another 10—I don't think we will attain it but we will begin funding them—it would be about $10 million in addition to the support we have in centers already.

Mr. OBEY. Unless I have misunderstood your response I don't think it answered my question. If you got $50 million more now, about how much of that addition would go into centers?

Dr. RAUSCHER. $10 million of the 50.

Mr. OBEY. Thank you, Doctor. That is all the questions I have for now.

TYPES OF CANCERS

Mr. FLOOD. Mr. Natcher.

Mr. NATCHER. Doctor, as I understand from your testimony, we have about 100 different kinds of cancer.

Dr. RAUSCHER. Correct.

Mr. NATCHER. Have you come to the conclusion that there are a great many things that might cause cancer and do cause cancer?

Dr. RAUSCHER. Yes, I have.

CAUSES OF CANCER

Mr. NATCHER. For a long time they talked in terms of a virus, that a virus was the cause of cancer. We have left that now have we, Doctor?

Dr. RAUSCHER. No, not by any means. I think the virology program——

Mr. NATCHER. I mean by that we are not saying all cancer results from a virus?

Dr. RAUSCHER. I have never felt that way and I think very few have.

Mr. NATCHER. So there are a great many things, as you have said to the committee, that could cause cancer. Now we read in the article that has been discussed here during the hearings today concerning red meats, and people that eat too much meat. Then we have articles that have appeared in the paper in the last few weeks concerning employees in plastic plants. So we would say then that a great many things could cause cancer, and, doctor, certainly I am not a doctor, but I believe when we discover what is causing cancer and does cause it we are going to find that there are so many causes and so many things that do cause cancer it is really going to be quite startling.

Dr. RAUSCHER. I think this must be true. I think there may be fewer common mechanisms by which different agents cause cancer. But certainly your point is well taken. There are probably hundreds of chemicals. We already know of 1,000 that cause cancer in animals. There are certainly viruses that are going to be found that cause human cancers. Not to mention physical factors, radiation and the like. Whether they all act on a common or several common pathways from the normal into the malignant is not known. But that gives us two ways to attack—the common pathways or the agents themselves. This is what we are working on.

SMOKING AND HEALTH

Mr. NATCHER. The National Cancer Act specifically authorizes you to encourage and coordinate cancer research by the private sector. I understand that, for the past 20 years the tobacco industry has funded about $60 million for independent scientific research and it is currently spending about $6 million a year. This is research in the field of smoking and health, much of it cancer research. Are you familiar with this body of research? And are you encouraging and coordinating it as the law specifically authorizes?

Dr. RAUSCHER. Yes, we are very familiar with this body of research. We are encouraging it and are coordinating its activities with ours. The national cancer program sponsors a special research effort in smoking and health, which maintains continuing liaison and benefits from the allied research programs funded directly or indirectly by the tobacco industry and other public and private organizations. Coordinating functions take place through the following:

The research directors of five major cigarette companies are full members of the NCI Tobacco Working Group, and advise the National Cancer Institute smoking and health program. They participate directly in the formulation of research.

Present and former NCI scientists served on the board of directors of the Council of Tobacco Research, a research funding agency sponsored by the tobacco industry. Continuing personal liaison is maintained on specific topics (particularly smoke inhalation devices) between Government, industry and Council for Tobacco Research specialists.

The National Cancer Institute specialists participate as advisors and observers in the formulation of joint research programs between the

University of Kentucky Tobacco and Health Research Institute and the Agricultural Research Service of the U.S. Department of Agriculture.

The National Cancer Institute maintains close liaison with research and action programs in smoking and health sponsored by the American Cancer Society, as well as liaison with the National Clearinghouse for Smoking and Health, the National Heart and Lung Institute and the U.S. Department of Agriculture.

The National Cancer Institute also maintains liaison and exchange of information with research in smoking and health sponsored by governments and private industry in England, Germany, France, Italy, Austria, and Japan.

OTHER FEDERAL AGENCIES INVOLVED IN CANCER PROGRAM

Mr. SHRIVER. Dr. Rauscher, you mention 12 other Federal agencies which are involved in the national cancer program. What are these other agencies, and what roles do they play?

Dr. RAUSCHER. Extensive coordination of Federal programs has existed for a number of years. Under the impetus of the National Cancer Act of 1971, National Cancer Institute has broadened interagency cooperation and joint efforts. There are at least 12 major Federal program areas that the national cancer program has included in the combined Federal responsibilities. These programs, in some instances are most strongly related to existing executive departments such as the Department of Health, Education, and Welfare while in others; particularly the more intensive areas, the coordination liaison involves a discrete organizational unit within a department or Federal organization.

The Food and Drug Administration and National Institute for Environmental Health Sciences have funded programs emphasizing research concerned with cancer causation. The Food and Drug Administration's work at the National Center for Toxicological Research and the Bureau of Biological Standards includes chemical and viral cancer causation and prevention activities. Support of cancer control activities has come from the Regional Medical Program Service, and a few projects on drugs and psychological aspects of cancer are funded by the National Institute for Mental Health. The National Institute for Occupational Safety and Health is pursuing research studies concerned with standards and control of carcinogens in the work environment.

Other agencies in the executive branch involved in national cancer program coordination include the Departments of Interior, Labor, and Transportation which have likewise pursued interests in aspects of the working conditions and environmental contents. Interior's effort has been concerned with the control of potential carcinogens affecting miners; while the Department of Labor's Occupational Safety and Health Administration has been concerned with enforcing standards for levels of carcinogenic material exposures to workers. The Environmental Protection Agency funds research related to controlling environmental carcinogens in the general environment. Because of important relationships of cancer and radiation, the Atomic Energy Commission conducts a full spectrum of research and control activities concerned with all aspects of radiation and cancer: basic research, causation, safety and prevention, diagnosis, and treatment. The National Aeronautics and Space Administration and the Department of Transportation likewise have funded a few projects on research on radiation. In responsibilities involving veterans, servicemen and their dependents, the Department of Defense and the Veterans' Administration have a wide variety of clinically oriented research and control activities and includes an important cancer pathology effort of the Armed Forces Institute of Pathology. The National Science Foundation supports many fundamental research projects important indirectly for the advance of cancer research. Several programs in the Department of Agriculture significant for cancer include research on tobacco, tumors and tumor-bearing animals, virology, genetics, metabolism and nutrition. Food, pesticides, herbicides, and other control programs are existing with Agriculture.

Many of the National Institutes of Health's Bureaus, Institutes, and Division support cancer-related research. The National Institute of Neurological Diseases and Stroke, the National Eye Institute, and the National Institute of Dental Research fund programs on brain, eye, and oral cancers. Virus-induced tumors are studied by the National Institute of Allergy and Infectious Diseases, and the Bureau of Health Manpower and Education has focused on the development of oncological nurses and other professionals. The National Library of Medicine is a significant resource. Most importantly, both formal and informal, interaction among scientists is encouraged from all of the Institutes.

ENVIRONMENTAL HAZARDS IN WORKPLACE

Mr. Shriver. Some of your new projects planned for 1975 include dealing with environmental hazards in the workplace. It seems like everyone is getting involved in this one. How are your efforts coordinated with Occupational Safety and Health Administration and the National Institute of Occupational Safety and Health? Are there other agencies also involved in this job safety program?

Dr. Rauscher. Through the Interagency Collaborative Group on Environmental Carcinogenesis, a mechanism of coordination has been established to work on problems involving exposure to chemical carcinogens in the workplace. Intensive coordination is especially evident with the Department of Labor—Occupational Safety and Health Administration—and the National Institute of Occupational Safety and Health, Communicable Disease Center, Department of Health, Education, and Welfare. This involves furnishing research reports, data from intramural and extramural projects and literature surveys—all as documenation on the hazard of exposure and the potential for cancer induction. As a resource for expertise on carcinogenesis, staff in the National Cancer Institute Carcinogenesis program provides technical advice and assistance to help Occupational Safety and Health Administration and National Institute of Occupational Safety and Health Administration in their decisionmaking processes. Additionally, we review, as requested, their standards and criteria documents.

With the implemention of Occupational Safety and Health Administration standards for fourteen carcinogens in the workplace—the number will increase in time—this occupational exposure and work safety problem has been extended to all laboratories. In this context, NCI now works with many agencies, both within the Department of Health, Education, and Welfare—Department of Transportation, Environmental Protection Agency, Food and Drug Administration, National Aeronautics and Space Administration, U.S. Department of Agriculture, Atomic Energy Commission, Department of Defense, and others. All of these have a common problem of insuring the safety of laboratory workers engaged in handling and investigating chemical carcinogens in laboratory studies.

COMMUNITY CANCER CENTER

Mr. Shriver. You mention that the first community cancer center has been established in Boise, Idaho, and that this should serve as a prototype for translating research findings into clinical practice in other communities which do not have a medical school. I'm sure there are other areas which would be interested in this. Would you discuss that further?

Dr. Rauscher. This is a relatively new development in the cancer centers program, but a growing number of communities are expressing interest and sending inquiries to our centers staff. Community centers are presently envisoned as cooperating adjuncts to our established cancer centers for research and demonstration. They will be able to furnish excellent cancer care to patients in communities of modest size which do not have a medical school, bringing to cancer patients, physicians, and paramedical personnel the benefits of the most recent advances in cancer research and treatment modalities.

The community centers will receive NCI support for cancer detection, education, research and the development and exchange of information but will also develop local sources of support for their programs and utilize normal sources of payment for patient care.

One community center is already funded and underway at the Mountain State Tumor Institute in Boise, Idaho. Two institutions—the Wilmington Medical Center in Delaware and the Luzerne County Medical Society in Wilkes-Barre, Pa.—are presently engaged in planning for such centers with NCI exploratory studies grant support. Applications for similar support have been received from the Kern Radiation Oncology Center in Bakersfield, Calif., and from the Greenville Hospital System in South Carolina. The number of such applications is expected to increase during fiscal year 1975.

VIRUS AS A CAUSE OF CANCER

Mr. Shriver. On page 5 you say, "no virus has yet been proven to cause human cancer." Last week, there was an article in the Washington Star-News concerning the so-called Zinder Report on your Institute's virus cancer program. After a year of study, Dr. Zinder was critical of the way in which your contracts are handled in virus research. Would you comment on that report, and tell us what, if any, changes you contemplate?

Dr. Rauscher. Although to some extent the report is based on a misunderstanding of the contract mechanism, I think it is basically a good report. A major issue in the report is the feeling that contracts do not receive the same high quality peer review that is true of the grant mechanism. The committee wanted to be sure that management aspects of the program are completely separate from the peer review process. The Institute has already taken steps to assure this separation and to assure that the program is totally open to new ideas and the best peer review available. Many of the remedies or modifications of the way in which this program is conducted, as recommended by the Zinder committee, will take place.

Mr. SHRIVER. Dr. Zinder also observed: "Basic ignorance of the mechanism involved in the cancer process, even in animals . . . is so profound that it is difficult to be certain where to begin, much less to organize a focused attack". Does that mean that we still really do not know what it is that causes cancer, or how whatever it is causes cancer?

I think it would be helpful for these hearings to include a brief discussion of the problems involved and the gaps in our knowledge in dealing with common forms of cancer, such as breast cancer or lung cancer. The public should know that it is going to be a long, hard struggle, rather than a quick, easy solution. Would you provide something for the record on that?

Mr. RAUSCHER. Yes, sir.

[The information follows:]

COMMON FORMS OF CANCER—PROBLEMS INVOLVED AND GAPS IN KNOWLEDGE

The Zinder report was referring to lack of knowledge of the mechanisms of development of cancer, not merely the identification of the causes. For instance, we do not know much about the mechanisms of action of smallpox virus on the body, but once it was identified as a cause, effective protection measures were developed. We, indeed, do know the causes of some cancers and have knowledge to prevent them. However, no human cancer virus has yet been identified.

Cancer is more than 100 separate diseases, although there are many common features between them. Conesquently, no single cause is probable nor does NCI assume one. There is not and never will be a single focused attack on cancer; there are and will be many attacks. The virus cancer program is only one.

The gaps in our knowledge of cancer are indeed many and with respect to lung cancer, our major cancer killer, we know what causes 80 percent of it and how it can be prevented—get people to stop smoking. Where the gap is in lung cancer is in effective treatment and knowledge of how to get people to stop smoking, or alternatively, to make a less hazardous cigarette.

With respect to breast cancer, the most frequent cancer in women in this country, the gaps are in both treatment and cause. We don't know with certainty which of several approaches to treatment of breast cancer will be best for an individual patient. Studies now underway will close that gap soon, I feel sure. The cause of human breast cancer is still unknown, although, again, certain types of viruses have been postulated. Viruses do cause breast cancer in mice. Improved methods of early detection have been developed and are now demonstration projects within the Institute's cancer control program. Early diagnosis will make most breast cancers curable by surgery.

ADEQUACY OF CANCER BUDGET

Mr. SHRIVER. You state: "The effective expansion of the national cancer program depends on adequate manpower and physical facilities." In your opinion, does this budget request represent an adequate amount for manpower and facilities?

Dr. RAUSCHER. The budget request for manpower is, I feel, adequate to support the present training activities of the Institute. In addition to fellowship and training grants, it includes $4 million for a new clinical education program for the upgrading and development of new curricula in the area of cancer education. We are also spending at a level of approximately $3 million for training and education under the cancer control program.

My advisers, including the National Cancer Advisory Board, the scientific community at large, and other individual scientists of international reputation have all indicated clearly that additional physical facilities to carry on the increased emphasis in cancer research are required. Further, provisions in the revised National Cancer Act will require us to initiate programs in biohazards control.

While this budget request may not provide funds sufficient to do all the construction desired, it does provide the resources to further expand our construction efforts for cancer research facilities.

UTILIZATION OF 1974 CONGRESSIONAL INCREASE

Mr. Shriver. In a related question, Congress provided an increase over the President's budget request last year of more than $30 million, even after the 5 percent cutback. How are you using those additional funds?

Dr. Rauscher. The total congressional increase over the President's budget was $51,191,500; however, as a result of the 5 percent reduction, the Institute received $23,632,000. This amount, plus $3.8 million for Federal pay increases and $3 million carried forward from 1973 for construction, represents the $30 million increase over last year's President's budget. The congressional increase of $23,632,000 (after the 5 percent reduction) is being utilized in the grants area and includes: $9.3 million for research grants; $6.7 million for fellowships and training grants; and $7.6 million for construction.

CONSTRUCTION

Mr. Shriver. Why are you limiting your construction funding to modernization and renovation of existing facilities? Is this a money-saving action, or is it based on the need?

Dr. Rauscher. Based on priority considerations within the budget, we have placed more emphasis on operational needs of cancer centers, the clinical education program, and expansion of the cancer control program. Therefore, we have reduced our estimate for construction from $45 million in 1974 to $22 million in 1975.

CANCERS TREATED

Mr. Shriver. You concluded your statement with the fact that advances in cancer research are responsible for the successful treatment of approximately 2½ million Americans, if things go as you now expect. That is the strongest justification I have heard for the appropriation of these funds.

Can you break that statistic down by types of cancer treated?

Dr. Rauscher. I will provide that information for the record.

[The information follows:]

Types of Cancer Treated

We have estimated that there are approximately 2½ million persons alive today who have survived at least 5 years after treatment for cancer. An additional 1 million cancer patients diagnosed and treated in the last 5 years are expected to live to join their ranks. The estimated breakdown of these 2½ million Americans by types of cancer treated is as follows:

Estimated number of successful cancer patients treated and alive today

Total, all sites	2,500,000
Breast	470,000
Colon and rectum	375,000
Head and neck (inc. lip)	225,000
Kidney and bladder	215,000
Prostate	205,000
Uterine cervix	190,000
Uterine corpus	165,000
Leukemia and lymphoma	95,000
Thyroid	70,000
Larynx	70,000
Lung	50,000
Ovary	50,000
Stomach	35,000
All other sites	285,000

OUTREACH PROGRAM

Mr. Conte. Do you have any kind of outreach program to family practitioners and nonspecialists in cancer to get better and earlier diagnosis?

Dr. Rauscher. The cancer control program has several projects underway directly relevant to this question. Currently under development is a project with the American Academy of Family Physicians. The study is concerned with the frequency of occurrence of approximately six different types of tumors as first seen in the family physician's office, and the feasibility of developing practical approaches to management that would include early diagnosis, treatment, and rehabilitation.

Second, seven projects are underway dealing with the early diagnosis and treatment of acute lymphocytic leukemia of childhood, Hodgkin's disease, and non-Hodgkin's lymphoma. The task of these projects is to identify patients with these disorders as early as possible and to bring them in so that optimal treatment can be provided. An additional task is to provide a program in continuing education to participating physicians. Through these projects, networks of contributing hospitals and practicing physicians have and still are being organized. The projects are located at Mt. Sinai Hospital, New York; Cornell University Medical Center, New York; Dartmouth Medical School, Hanover; Children's Hospital, Cincinnati; University of Alabama, Birmingham; Children's Hospital, Denver; and Children's Hospital, Los Angeles. It is planned that the work-scope of these projects will be expanded to include other hematological malignancies.

Third, approximately 15 projects concerned with head and neck cancers, and breast cancer, are being developed and will be awarded by the end of this fiscal year. The objective is to develop similar networks of practicing physicians and hospitals so that better and earlier diagnosis, and more effective treatment and rehabilitation can be effected.

In addition, 10 grants will be awarded by the end of this fiscal year to various NCI comprehensive cancer centers and clinical cooperative groups to develop outreach networks that will include practicing physicians and community hospitals. Again, the objective is to effect early diagnosis and optimal treatment and rehabilitation.

Collateral to these specific efforts are additional projects concerned with the training of oncology nurses in all aspects of cancer, from early detection, through diagnosis and treatment. The cervical cytology screening program with State health departments is also developing a relationship with family practitioners.

SURVIVAL RATES

Mr. CONTE. Where are you getting the most significant changes in survival rates—in terms of kinds of cancer and of different population groups?

Dr. RAUSCHER. Data indicate that prognosis for female patients is considerably better than that for males. For patients diagnosed between 1955–64, 5-year relative survival rates were 42 and 31 percent respectively for females and males. This differential is due in part to the fact that somewhat poorer prognosis is associated with the most frequently occurring cancer sites in men. Furthermore, women have a survival advantage over men for many cancer sites that occur in both sexes.

Significant improvements in 5-year survival rates have occurred for prostatic cancers, Hodgkin's disease, multiple myeloma and melanoma of the skin.

Data on survival for childhood cancer (under 15 years of age) now being prepared for publication show there has been improvement over time. One year relative survival rates have progressively increased from 50 percent in 1955–59 to 70 percent in 1970–71. The most significant improvement in survival has been for children with leukemia for whom 1-year survival rates have increased from a low of 31 percent in 1955–59 progressively to a high of 73 percent in 1970–71. For acute lymphocytic leukemia, the increase in 1-year rates over the same time period was from 30 to 80 percent. Some improvements in survival, through less dramatic, have been observed for children with brain tumors and lymphomas.

Other data in preparation for publication indicate that survival for white cancer patients is more favorable than for black patients. The largest differences were observed for the forms of cancer with the best prognoses: bladder, larynx, and uterine corpus. For more lethal forms, such as leukemia and lung cancer, there were small racial differences in survival. For males diagnosed with bladder cancer during 1955–64, the 5-year survival differential was 56 percent for white versus 29 percent for black patients. Similar results were observed for women with bladder cancer. White men with cancer of the larynx experienced a 56 percent 5-year survival rate compared with 44 percent for black male patients. For women with larynx cancer, the survival differential was negligible. The 5-year survival differential by race for cancer of the corpus was 72 percent versus 40 percent for white and black women, respectively.

CANCER RESEARCH IN OTHER INSTITUTES

Mr. CONTE. Will you identify the research areas in other Institutes most directly relevant to cancer? What impact will their steady, or reduced, budgets have on progress against cancer?

Dr. RAUSCHER. Most, if not all, of the other institutes are conducting or supporting research relating directly or tangentially to the mission of NCI. This is due to the fact that NCI and the other Institutes share a broad community of scientific interests. Cancer arises in all of the organ systems being studied by other Institutes. Moreover the neoplastic process represents abnormalities in the cellular, subcellular, physiologic, metabolic, and genetic processes that are involved in the genesis of the full range of human diseases. Thus the basis for progress against cancers depends not only on the application of existing scientific knowledge, but also on the continuing elucidation of normal and abnormal biologic process. These fundamental probes with relevance to cancer are conducted and supported by all of the Institutes, not just the NCI; in like fashion the studies supported by NCI are likely to have great relevance to the disease-centered interests of other Institutes.

The following thrusts of other Institutes illustrate research areas with direct relevance to cancer:

NHLI—Lipid metabolism (proposed role of fat in the causation of certain human cancers); lung diseases (lung cancer is responsible for the greatest number of cancer deaths); and blood diseases (relationship of blood coagulation factors to cancer growth and spread).

NIAID—Transplantation and immunology (factors which relate broadly to the cause, prevention, diagnosis, and treatment of cancer); and virology (impacts directly on one of the major factors involved in cancer causation).

NIAMDD—Nutrition (an area of increasing potential significance in respect to cancer causation); and molecular biology (a basic field which is shedding light on mechanisms of cancer causation as well as approaches for cancer prevention, detection, and treatment).

NICHD—Molecular genetics (a field which can provide insights concerning mechanisms of cancer induction, prognosis, and response to treatment); and aging (may provide information illuminating the role that the aging cell and organism may play in the onset, prevalence, and progress of the neoplastic process).

NIDR—Oral cancer (a subject of direct relevance to NCI interests).

NIEHS—(The interests of this Institute and NCI, particularly in terms of chemical carcinogenesis, broadly coincide).

NIGMS—Genetics (an extensive and broadbased program with great potential relevance to the factors underlying the initiation and expression of cancers); cellular and molecular bases of disease; and biomedical engineering.

NINDS—Virology (viruses may play a part in a number of puzzling neurologic diseases. The nature of such "slow viruses," the mechanisms through which they may induce disease and their possible relation to cancer-causing viruses are being explored); and brain tumors (an area of immediate relevance to NCI activities).

The above list is representative and not exhaustive. It illustrates the conceptual and practical relationship of the activities of the Institutes of NIH. The boundaries seemingly imposed by the existence of several Institutes are apparent and not real, since there is a true collaboration and interdependence among the scientists working in a variety of disciplinary areas.

Reduced or steady budgets (which in the face of continuing inflationary pressures amount to reductions) for any of the other Institutes can only serve to reduce the vigor and productivity of this cooperative scientific effort which generates the new leads which all of the Institutes strive to translate into progress against cancer and a multitude of other diseases.

Mr. CONTE. What are the central academic disciplines from which cancer researchers are drawn?

Dr. RAUSCHER. These disciplines are biochemistry, cancer biology (cell transformation and cell genetics), carcinogenesis, chemistry, clinical oncology, drug development and chemotherapy, epidemiology and biostatistics, immunology, molecular biology, viral and microbiology, and other biological sciences.

Mr. CONTE. Do you project any shortages in those disciplines?

Dr. RAUSCHER. Yes, it is anticipated that a shortage will exist in those disciplines. We are attempting to alleviate this shortage through our fellowships and training grants programs, a new clinical education program and through an expanded educational effort in our cancer control program.

Mr. CONTE. On the average, how many years training after the B.A., and at what cost, are required for a research career?

Dr. RAUSCHER. Approximately 6 years of training, 4 years graduate and 2 years postdoctoral are required.

Mr. CONTE. What is the average cost of that training?

Dr. RAUSCHER. About $14,500 a year.

Mr. CONTE. How much of that cost will your new fellowships cover?

Dr. RAUSCHER. The new fellowships will cover the total cost for postdoctoral training of which about $11,500 is for investigator support and the balance for the institution. None of the predoctoral training costs would be supported.

Mr. CONTE. What is the average salary of a biomedical researcher in the first 5 years after training?

Dr. RAUSCHER. For an M.D. it is about $27,500 and for Ph. D. or D.V.M. it is about $16,000.

VIRAL CAUSES OF CANCER IN ANIMALS

Mr. CONTE. In how many different animal species do you have evidence of viral causes of cancer?

Dr. RAUSCHER. There is definite evidence for the viral causation of cancer in the following animal species: snake, frog, chicken, mouse, rat, hamster, guinea pig, rabbit, cat, cow and subhuman primates (monkey, ape). I would like to insert for the record a list of viruses known to cause cancers in animals including certain viruses associated with human cancers.

[The information follows:]

Viruses That Produce Cancers in Animals

COMMON NAME OF VIRUS	NO. OF MAJOR ISOLATES	HOST OF ORIGIN	PRODUCES NEOPLASIA IN:	TUMOR TYPE IN ANIMALS
Mouse Leukemia	17	Mouse	Mice, Rats, Hamsters, TC	Leukemia, Lymphoma
Mouse Leukemia (endogenous)	4	Mouse	TC, To be determined	To be determined
Mouse Sarcoma	4	Mouse	Mice, Rats, Hamsters, Cats, TC[1]	Sarcomas
Polyoma	2	Mouse	Mice, Hamsters, TC	All types except Leukemia
Mammary tumor	Several[2]	Mouse	Mice	Carcinoma
Chicken Leukemia	4	Chicken	Chicken	Leukemia
Twiehaus or RE	4	Chicken, Duck	Chicken, Quail, Hamster, Duck	Reticuloendotheliosis
Chicken Sarcoma	9	Chicken	Chicken, Quail, Turkey, Duck, Hamster, Monkey, TC, etc.	Sarcoma
Marek's	4	Chicken	Chicken	Lymphoma
CELO	1	Chicken	Hamster	Sarcoma
Cat Leukemia	4	Cat	Cat	Leukemia, Lymphoma
Cat Leukemia (endogenous)	1	Cat	To be determined	To be determined
Cat Sarcoma	4	Cat	Cat, Dog, Rabbit, Monkey, Marmoset	Sarcoma

COMMON NAME OF VIRUS	NO. OF MAJOR ISOLATES	HOST OF ORIGIN	PRODUCES NEOPLASIA IN:	TUMOR TYPE IN ANIMALS
Shope Papilloma	1	Rabbit	Rabbit	Papilloma
Dog Mast Cell	1	Dog	Dog	Mastocytoma
Lucké	1	Frog	Frog	Carcinoma
Human Adeno	31[3]	Man	Hamster, Mice, TC	Sarcoma
Wart	1	Man	Man	Papilloma
Hybrids[4]	>7	Monkey, Man, Cat, Mouse, Hamster, Rat	Hamster, TC	Sarcoma
Yaba	1	Monkey	Monkey, Man	Histiocytoma
H. Saimiri	1	Monkey	Monkey	Lymphoma
H. Ateles	1	Monkey	Monkey	Lymphoma
H. Sylvagicus	1	Rabbit	Cottontail Rabbit	Lymphoma
Simian Adeno	6	Monkey	Hamster, TC	Sarcoma-Lymphoma
SV 40	1	Monkey	Hamster, Mice, TC	Ependymoma, Sarcoma, Carcinoma
Graffi Hamster	2	Hamster	Hamster	Lymphoma, Papilloma
Bovine Papilloma	1	Cow	Cow, Horse, Mouse, Hamster	Papilloma, Fibroma
Bovine Leukemia	2	Cow	To be determined	To be determined
HSV-1	1	Man	TC, To be determined	To be determined
HSV-2	1	Man	TC, To be determined	To be determined

COMMON NAME OF VIRUS	NO. OF MAJOR ISOLATES	HOST OF ORIGIN	PRODUCES NEOPLASIA IN:	TUMOR TYPE IN ANIMALS
Cytomegalo	3	Man	TC, To be determined	To be determined
EBV	1	Man	TC, Marmoset	Lymphoma
R-35 Rat	1	Rat	To be determined	To be determined
MP-MV	3	Monkey, Man	To be determined	To be determined
Woolly monkey Fibrosarcoma	1	Woolly monkey	Woolly monkey, Marmoset, TC	Fibrosarcoma
Gibbon Leukemia	2	Gibbon	To be determined	To be determined
Baboon	2	Baboon	To be determined	To be determined
Rhesus monkey (placenta)	1	Rhesus monkey	To be determined	To be determined
Human (placenta)	1	Man	To be determined	To be determined
SA-4	1	Man	To be determined	To be determined
	134[3]			

1/ TC = Tissue Culture

2/ Antigenic differences among isolates not yet determined.

3/ Approximately 12 of 31 human adeno viruses induce malignancies in hamsters. These 12 and the remaining 19 induce discrete foci of transformed (apparently cancerous) cells in tissue cultures.

4/ Hybrid = Genotypic recombinates of 2 different viruses; e.g., SV40 + Adeno.

Mr. CONTE. Which of those species are closest to humans in the kinds of cancer they develop?

Dr. RAUSCHER. In the mammalian species, viruses which contain RNA or DNA as genetic material induce leukemias, lymphomas, sarcomas, and carcinomas which are histologically similar to diseases in man. Viruses isolated from different species are not identical; however, they are related to each other biochemically and immunologically. The virus cancer program is emphasizing studies on primate viruses because available evidence indicates that their characteristics will be more nearly like those of the human viruses.

HUMAN RESEARCH

Mr. CONTE. With ethical considerations on research with humans, how are you going to close this gap between animal and human research on viral cancer causes?

Dr. RAUSCHER. Research on animal systems has provided biochemical and immunological markers to use in the search for human tumor viruses. Studies on blood and tissue of cancer patients obtained after surgery or on autopsy provide the starting reagents for this search. When found, viruses can be tested for their ability to induce malignant changes in closely-related animal species or in human cells growing in tissue culture. Similarly, any agents which block or control malignancy biochemically will be screened and tested in animals and in human cells in culture. The efficacy and safety of methods for reducing or preventing the incidence of cancers immunologically will also be thoroughly studied in suitable animal systems before human application. For example, if a modified viral vaccine is used, it will not contain components capable of replicating or inducing malignancy in man. Therefore, there are no serious ethical obstacles to closing the gap between animal and human research on virus induced cancers.

GENETIC COUNSELING

Mr. CONTE. What kinds of genetic counseling are being carried out with what kinds of high risk groups?

Dr. RAUSCHER. At the present time, no genetic counseling is being done. However, we do have one project under consideration concerned with the incidence and natural history of genital tract anomalies and cancer in offspring exposed *in utero*. The high risk groups in this study are several identified populations of teenage girls who were exposed *in utero* to diethylstilbestrol taken by their mothers. The counseling involved in this study is not genetic per se, but certainly there is a similarity. It is anticipated that the Institute will further its genetic counseling efforts in subsequent years.

Mr. ROBINSON. Would you supply for the record the extent to which cancer investigations are being supported in Virginia with Federal funds?

I have in mind, in particular, work at the Medical Center of the University of Virginia and the Medical College of Virginia, but I should be interested, as well, in other Federally-supported efforts in Virginia.

Dr. Rauscher. I will provide that information for the record.

[The information follows:]

FEDERAL CANCER SUPPORT IN VIRGINIA

	Number	Amount
Virginia Commonwealth University (Medical College of Virginia), Richmond:		
(a) Research grants	14	$728,599
(b) Training grants	3	116,935
Subtotal		845,534
University of Virginia, Charlottesville:		
(a) Research grants	12	623,518
(b) Training grants	2	71,022
(c) Research contracts	2	184,674
Subtotal		879,214
Virginia Polytechnical Institute and State University, Blacksburg:		
(a) Research grants	2	49,638
(b) Research contracts	1	200,000
Subtotal		249,638
Nonprofit:		
(a) Research contracts	1	225,000
Subtotal		225,000
Profit:		
(a) Research contracts	26	5,870,904
Subtotal		5,870,904
Summary: —		
Research grants	28	1,401,755
Training grants	5	187,957
Research contracts	30	6,480,578
Total, Federal (NCI) cancer support in Virginia		8,070,290

Mr. Robinson. There was reported in the press today an estimate by a researcher of some repute that two viruses causal to cancer would be identified within the next year. Do you see a prospect of this?

Dr. Rauscher. I will provide that information for the record.

[The information follows:]

Viruses That Induce Cancer

The impressive progress in the understanding of RNA tumor virus replication has provided new ways of searching for virus information in human cancers. Very recent and highly interesting biochemical data indicate that particles, found associated with human leukemias and with human breast cancer, contain specific proteins not found in normal tissue or other kinds of human cancer. These proteins also show relationships to components of known oncogenic animal viruses. It is reasonable, therefore, to assume that the two particles will be isolated and characterized within the next year.

The protein products can be useful in the early diagnosis of the disease, in monitoring patient therapy, and in screening groups at high risk to develop these cancers. Since these proteins are associated with a virus or virus-like particle, they could potentially be employed in developing specific immunotherapy for these diseases.

Mr. Flood. Thank you, Dr. Rauscher.

Dr. Rauscher. Thank you, Mr. Chairman.

JUSTIFICATION OF THE BUDGET ESTIMATES

NATIONAL INSTITUTES OF HEALTH

National Cancer Institute

Amounts Available for Obligation 1/

	1974 Revised	1975
Appropriation	$551,191,500	$600,000,000
Amount withdrawn (PL 93-192)	23,705,500	---
Subtotal, adjusted appropriation	527,486,000	600,000,000
Real transfer to:		
"Departmental management" (To centralize public information functions)	-180,000	---
Comparative transfers to:		
"Office of Assistant Secretary for Health" (Transfer of administrative support activities to the Office of the Assistant Secretary for Health)	-193,000	---
"Departmental management" (For Department-wide reductions in public affairs)	-25,000	---
Comparative transfers from:		
"Departmental management" (Transfer of indirect cost negotiation function to the OS Working Capital Fund)	+32,000	---
"National Institute of General Medical Sciences" (Decentralization of scientific evaluation grants program)	+279,000	---
Subtotal, budget authority	527,399,000	600,000,000
Unobligated balance, start of year	2,990,000	---
Total, 1974 base obligations	530,389,000	600,000,000
Unobligated balance, restored	58,859,000	---
Comparative transfer of restored unobligated balance to Research Resources for General Research Support Grants	-776,000	---
Total, obligations	588,472,000	600,000,000

1/ Excludes the following amounts for reimbursable activities carried out by this account: 1974 - $31,000; 1975 - $31,000.

Summary of Changes

1974 Estimated obligations	$588,472,000
1975 Estimated obligations	600,000,000
Net change	+11,528,000

	Base		Change from Base	
	Pos.	Amount	Pos.	Amount
Increases:				
A. Built-in:				
1. Annualization of new positions in 1974	---	---	---	+$1,131,000
2. Annualization of 1974 pay increase	---	---	---	+474,000
3. Within-grade pay increases	---	---	---	+530,000
4. Wage-board pay increases	---	---	---	+57,000
5. Extra day of pay	---	---	---	+132,000
6. Bureau of Employees Compensation	---	---	---	+13,000
7. FTS rate increase	---	---	---	+47,000
8. Service and Supply	---	---	---	+83,000
9. Payment to NIH Management Fund	---	$16,940,000	---	+899,000
Subtotal	---	16,940,000	---	+3,366,000
B. Program:				
1. Research grants				
a. Non-competing continuations - regular program	---	64,532,000	---	+28,049,000
b. Competing (new, continuations, and supplementals)	---	50,621,000	---	+40,628,000
c. Special programs	---	104,036,000	---	+18,874,000
2. Fellowships				
a. Non-competing continuations	---	454,000	---	+5,403,000
b. Competing (new, continuations, and supplementals	---	6,631,000	---	+6,550,000
3. Training grants				
a. Non-competing continuations	---	12,259,000	---	+4,000,000
4. Intramural laboratory and clinical research	509	16,265,000	+7	+330,000
5. Research and development contracts	---	180,369,000	---	+125,000
6. Collaborative research and support	894	34,399,000	+12	+1,963,000

Summary of Changes--continued

	Base		Change from Base	
	Pos.	Amount	Pos.	Amount
Increases:--continued				
B. Program:--continued				
7. Research management and program services.........	405	18,579,000	+11	+4,485,000
8. Cancer control.............	30	34,055,000	+5	+10,911,000
Subtotal....	1,838	522,200,000	+35	+121,318,000
Total, increases.........			+35	+124,684,000
Decreases:				
A. Program:				
1. Research grants				
a. Non-competing completed or converted to competing status.....			---	-18,069,000
b. Competing completed or converted to non-competing............			---	-45,671,000
c. 1974 obligations used to fund 1975 continuations........			---	-4,950,000
2. Fellowships				
a. Non-competing completed or converted to competing status.....			---	-341,000
b. Competing completed or converted to non-competing............			---	-6,631,000
3. Training grants				
a. Non-competing completed or converted to competing status.....			---	-10,162,000
b. Competing completed or converted to non-competing............			---	-4,299,000
4. Construction..............	---	45,033,000	---	-23,033,000
Total decreases..........				-113,156,000
Total, net change....................	---	---	+35	+11,528,000

Explanation of Changes

Increases:

A. Built-in:--These increases will provide: $1,131,000 for annualization of new positions in 1974; $474,000 for annualization of 1974 pay increases; $530,000 for within-grade pay increases; $57,000 for wage-board pay increases; $132,000 for an extra day of pay; $13,000 for increased contribution to the Bureau of Employees Compensation; $47,000 for increased costs for use of the Federal Telecommunications System; $83,000 for increased costs to the Service and Supply Fund and $899,000 for increased support to the NIH Management Fund.

B. Program:

1. Research grants

a. The increase of $28,049,000 in non-competing regular research grants represents the increased costs for continuation in 1975 of competing continuations and new research grants funded in 1974.

b. The amount of $40,628,000 in competing research grants reflects: (a) $20,265,000 for 325 new awards; (b) $16,837,000 for 208 competing continuations; and (c) $3,526,000 in supplementals.

c. The increase of $18,874,000 represents: an increase of $13,039,000 for expansion of the cancer research centers program which will provide for expansion and strengthening of both comprehensive and specialized research centers; $997,000 for expanded task force efforts related to cancer of the large bowel, bladder and prostate; $47,000 for scientific evaluation grants; $4,000,000 for a new Clinical Education Program for awards to educational institutions to provide more innovative teaching programs related to cancer research; $890,000 for research into the application of high LET radiation for use in cancer patients; and a decrease of $99,000 in research career awards.

2. Fellowships

a. The amount of $5,403,000 in non-competing fellowships represents an increase over the 1974 non-competing level for the 1975 cost of continuing previously awarded competing and non-competing fellowships in 1974. Total non-competing fellowships will increase by 352 over the 42 in 1974.

b. The amount of $6,550,000 in competing fellowships represents the level of support for 536 fellowship awards in 1975.

3. Training grants

a. The amount of $4,000,000 in non-competing training grants represents the increase for continuation costs of previously funded training grants.

4. Intramural laboratory and clinical research--The program increase of seven positions and $330,000 will allow for increased research efforts in the detection and diagnosis of cancer, particularly in the area of immunology research.

5. Research and development contracts--The program increase of $125,000 will still permit efforts in the search for viruses which cause cancer in man; expansion in the madalities of cancer therapy particularly combined modalities; increased research in the carcinogenic potential of selected chemicals; further efforts in the role of immunology in cancer research; and modest expansion of task force efforts related to cancer of the breast and lung.

Explanation of Changes--continued

Increases:--continued

B. Program:--continued

6. Collaborative research and support--The program increase of 12 positions and $1,963,000 will permit a modest expansion of in-house research efforts and contract management in the areas of cause and prevention research and treatment research, including task force efforts in breast and lung cancer.

7. Research management and program services--The program increase of 11 positions and $4,485,000 will provide resources to support the expanded activities of the Institute called for by the National Cancer Act. Increases in this area will include support for: the overall administration and guidance to the National Cancer Program; expanded international research activities including an International Cancer Research Data Bank; further updating and refinement of the National Cancer Program Plan; and increased support for the management and administration of both research contracts and grants.

8. Cancer Control--The program increase of five positions and $10,911,000 will allow expansion of the Institute's cancer control activities including the 27 centers established for the early detection of breast cancer, as well as other efforts in the prevention, screening, diagnosis, treatment, rehabilitation, and education related to cancer research.

Decreases:

A. Program:

1. Research grants

a. The decrease of $18,069,000 represents 288 non-competing regular research grants that were completed in 1974 or that are being converted to competing status in 1975.

b. The decrease of $45,671,000 represents the completion or conversion to non-competing status of 626 competing grants.

c. The decrease of $4,950,000 reflects the reduction of funds needed in 1975 as a result of the funding of 80 grants in 1974.

2. Fellowships

a. The decrease of $341,000 represents the completion of 32 fellowships in 1974.

b. The decrease of $6,631,000 represents the completion or conversion to non-competing status of 500 competing grants.

3. Training grants

a. The decrease of $10,162,000 represents the completion of training grants in accordance with the phase out of this program when training under previously approved training grants is completed.

b. The decrease of $4,299,000 represents the completion or conversion to non-competing status of 207 training grants.

4. Construction--The program decrease of $8,483,000 will still allow resources for the modernization and renovation of existing space for cancer laboratory and clinical research purposes. The additional $14,550,000 decrease represents the restoration of 1973 impounded funds.

Obligations by Activity

Page Ref.		1974 Base* Pos.	1974 Base* Amount	1975 Estimate Pos.	1975 Estimate Amount	Increase or Decrease Pos.	Increase or Decrease Amount	
24	Research							A
	(a) Cause and prevention research.......	638	$133,481,000 (145,860,000)	647	$151,662,000	+9	+$18,181,000	
	(b) Detection and diagnosis research.......	161	37,249,000 (39,244,000)	168	41,744,000	+7	+4,495,000	
	(c) Treatment research.......	647	178,674,000 (194,402,000)	653	203,128,000	+6	+24,454,000	
	(d) Cancer biology...	317	77,488,000 (85,439,000)	321	89,321,000	+4	+11,833,000	
37	Resource development							B
	(a) Cancer centers support........	12	19,578,000 (19,578,000)	14	23,484,000	+2	+3,906,000	
	(b) Research manpower development....	8	18,530,000 (24,010,000)	8	22,530,000	---	+4,000,000	
	(c) Construction.....	11	30,790,000 (45,340,000)	11	22,317,000	---	-8,473,000	
42	Cancer control							C
	(a) Cancer control...	44	34,599,000 (34,599,000)	51	45,814,000	+7	+11,215,000	
Total obligations (base)..		1,838	530,389,000	1,873	600,000,000	+35	+69,611,000	
Total obligations.........			(588,472,000)					

Explanation of Changes

A) Research

a) Cause and prevention research--In addition to the built-in increase of $1,041,000, the program increase of nine positions and $17,140,000 will permit the exploitation of existing research efforts as well as significant new research leads including: the exploration of cancer-causing viruses in man; the further development of a screening test that may identify cancer-causing chemicals in a matter of weeks compared to two to three years; expanded epidemiological research on the potential effects of air pollution on lung and stomach cancer; and further expansion of the present research advances through the task force programs relative to the causative factors of cancer.

*Excludes 1973 appropriation restorations.

b) Detection and diagnosis research--In addition to the built-in increase of $271,000, the program increase of seven positions and $4,224,000 will permit further improvement of both the methods and equipment for the x-ray diagnosis of cancer; ultrasonic scanning, which may be able to screen for breast cancer without the potential hazard of x-irradiation; and accelerated efforts in the field of immunodiagnostic procedures which will provide a means of identifying specific tumors while they are small enough to be treated with an expectation of obtaining a cure.

c) Treatment research--In addition to the built-in increase of $1,324,000, the program increase of six positions and $23,130,000 will permit an accelerated effort in the search for drugs with activity against slow growing tumors; further exploration of the combinations of therapeutic methods of treatment for cancer tumors, especially the common solid tumors of the breast, lung and colon; increased emphasis on Phase II (therapeutic effectiveness) studies in order to decrease the time loss in evaluation of combination therapy; and the screening of 50,000 materials for antitumor activity.

d) Cancer biology--In addition to the built-in increase of $538,000, the program increase of four positions and $11,295,000 will provide for the further development of the scientific base relative to the causes and nature of cancer, with the expectation that this will result in better prevention, detection and diagnosis, and treatment methods. Included within this activity is research that cannot reasonably be classified in any one of the other research thrusts, but where output has potential application to all thrusts.

B) Resource development

a) Cancer centers support--In addition to the built-in increase of $28,000, the program increase of two positions and $3,878,000 will provide the resources for expansion of both exploratory projects and the core support portion of cancer research centers. Exploratory projects are designed to determine the feasibility of establishing cancer centers and to support planning efforts. The core grants support the administration, common services and collaborative activities of cancer centers. The research performed within the cancer centers program is incorporated in the activity - Research.

b) Research manpower development--In addition to the built-in increase of $19,000, the program increase of $3,981,000 will continue to support the research training and fellowships program as well as permit the initiation of a clinical education program.

c) Construction--In addition to the built-in increase of $10,000, there is a program decrease of $8,483,000 to a level of $22,317,000, which will still allow resources for the modernization and renovation of existing space for cancer laboratory and clinical research purposes.

C) Cancer Control

a) Cancer control--In addition to the built-in increase of $135,000 the program increase of seven positions and $11,080,000 will permit the expansion and initiation of additional efforts relative to bridging the gap between the discovery of effective research findings and their application in the practice of medicine and public health. Included in this effort is an increase of seven demonstration centers for breast cancer detection as well as significant increases in the diagnosis and treatment aspects of this program.

Obligations by Object

	1974 Estimate	1975 Estimate	Increase or Decrease
Total number of permanent positions........................	1,838	1,873	+35
Full-time equivalent of all other positions..................	156	165	+9
Average number of all employees........................	1,955	2,011	+56
Personnel compensation:			
Permanent positions..............	$29,265,000	$31,278,000	+$2,013,000
Positions other than permanent....	1,505,000	1,585,000	+80,000
Other personnel compensation......	859,000	885,000	+26,000
Subtotal, personnel compensation.................	31,629,000	33,748,000	+2,119,000
Personnel benefits.................	3,537,000	3,750,000	+213,000
Travel and transportation of persons..........................	2,150,000	2,300,000	+150,000
Transportation of things...........	335,000	365,000	+30,000
Rent, communications and utilities........................	1,800,000	2,200,000	+400,000
Printing and reproduction..........	900,000	975,000	+75,000
Other services:			
Project contracts.................	215,502,000	219,917,000	+4,415,000
Payment to NIH Management Fund....	16,940,000	17,839,000	+899,000
Other..........................	14,047,000	18,943,000	+4,896,000
Supplies and materials.............	12,000,000	13,200,000	+1,200,000
Equipment........................	3,900,000	4,150,000	+250,000
Grants, subsidies and contributions....................	285,732,000	282,613,000	-3,119,000
Total obligations by object.....	588,472,000	600,000,000	+11,528,000
Total obligations excluding 1973 appropriation...........	530,389,000		

Significant Items in House and Senate Appropriations Committee Reports

Item	Action taken or to be taken
1974 House Report	
Program Balance	
1. The Committee wants to be assured that the NCI program maintains a proper balance between exploratory, free-wheeling, investigator-directed projects and the developmental, contractually defined, committee directed projects (page 26).	1. NCI is continually reviewing this relationship. During the past year, the President's Cancer Panel and the National Cancer Advisory Board have specifically reviewed this matter of program balance and the funding mechanisms. This budget has been prepared in accordance with the recommendations of the Panel and Board.
Comprehensive Cancer Centers	
2. The Committee felt that in view of the central role which these centers are expected to play, the full number of centers must be established as soon as possible and that their needs must be fully met. The Committee stated that one of the most important new authorities in the new Cancer Act is the provision to establish 15 comprehensive centers. The Committee was assured that all 15 centers will be in operation by the end of fiscal year 1974 (page 27).	2. Nine of the 15 comprehensive centers have already been selected and the remaining six will be selected and in operation by the end of fiscal year 1974. This will bring the total of comprehensive centers to 18, since there were three identified as comprehensive centers at the time of passage of the National Cancer Act of 1971.
Exploratory Grant Program	
3. The Committee directed that $6 million be used for the specific purpose of expanding the Exploratory Grant Program which is used for the advance planning of specialized and comprehensive cancer centers (page 27).	3. Funds utilized for this purpose in 1974 will total approximately $6 million through the Exploratory Grant Program, as well as through planning efforts included with operational funds provided to the new comprehensive cancer centers.
Cancer Control Program	
4. The Committee was impressed with the plans for this program. However, the Committee was not impressed with past efforts to involve local practicing physicians in cancer control. The NCI should make every effort to involve local physicians in the National Cancer Program. The Committee also recognized that the Cancer Control Program is an important and essential component of the Cancer Center and accordingly should be supported by both grants and contracts (page 28).	4. One of the major objectives of the Cancer Control Program is to bring cancer research findings to practicing physicians. Efforts to demonstrate these findings to the medical community are currently under way and they will be expanded in the future. A major characteristic of the comprehensive cancer centers is that they will have an outreach to the local community and practicing physicians. The Cancer Control Program is now being funded through both grants and contracts.

Item	Action taken or to be taken
1974 House Report	
Program Review Mechanisms	
5. It was the expressed hope of the Committee that NCI develop program review mechansims which elicit, in planning and operation, the active participation of representatives from the lay community, private physicians, and private cancer specialists (page 28).	5. Increasing efforts are being made to involve private cancer specialists and private physicians in the various NCI program-review mechanisms. All major areas of the Institute now have advisory committees with membership which includes private cancer specialists, private physicians and representatives from the lay community. These advisory committees are playing an increasing role in reviewing the programs of the national cancer effort.
1974 Senate Report	
Cancer Control Program	
1. The Committee considered the Cancer Control Program to be one of the most important activities called for by the new Cancer Act. Every effort must be made to demonstrate effective research findings in the community (page 39).	1. The major objective of this program is to demonstrate cancer research findings to the public and practicing physicians. The Cancer Control Program is now fully operational and a 1975 increase of $11,215,000 is being requested for a total of $45,814,000.
Frederick Cancer Research Center	
2. The Committee was interested in the Frederick Cancer Research Center including the new initiatives in animal reproduction, production of antibiotic materials used in cancer research and other related areas (page 39).	2. A major portion of the Institute's bioassay needs for research animals are now supplied from this facility. Plans are under way to produce antibiotic materials at this facility for the Institute's cancer treatment research program.
Immunology	
3. The Committee was pleased with the establishment of a major research program in tumor immunology. This promising program should be continued and expanded in 1974 (page 40).	3. NCI has taken steps to give the immunology program increased emphasis. Activities have been initiated to expand and coordinate the Institute's efforts in this promising field. An Associate Director for Immunology has been designated with overall responsibility for directing and coordinating the activities of the program.

Item	Action taken or to be taken
1974 Senate Report	
Norris Cotton Cancer Research Center	
4. The Committee earmarked funds for this center so that it could become a full-fledged comprehensive cancer research center (page 41).	4. Plans have been initiated to upgrade and expand this facility from a specialized cancer radiation center to a comprehensive cancer research center.
Positions in NIH Clinical Center	
5. The Committee recognized that there is a critical shortage of positions needed for patient care within the Clinical Center and could not accept such cutbacks (page 41).	5. Cooperative efforts are under way to explore possible solutions to the shortage of personnel. The Clinical Center is not an organizational part of NCI, although it provides NCI with invaluable laboratory and patient care facilities and services. NCI will continue to work with Clinical Center staff and NIH management concerning the staffing problems at the Clinical Center.

Authorizing Legislation

Legislation	1975 Authorization	1975 Appropriation requested
Public Health Service Act:		
Title IV, Part A -- National Cancer Institute...........................	1/	$600,000,000

1/ Authorization expires June 30, 1974: extension legislation is proposed.

National Cancer Institute

Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
1965	$134,947,000	$134,203,000	$143,534,000	$143,534,000
1966	148,709,000	152,359,000	158,074,000	158,609,000
1967	158,581,000	164,863,000	169,863,000	169,863,000
1968	176,246,000	176,246,000	183,941,000	176,225,000
1969	180,869,000	175,754,000	184,754,000	178,311,500
1970	173,887,000	173,887,000	191,703,000	183,648,063
1971	197,404,000	220,651,000	228,651,000	223,651,000
1972	369,063,000	371,479,000	391,469,000	372,881,000
1973*	427,335,000	485,418,000	435,418,000	485,418,000*
1974	499,913,000	522,296,000	579,913,000	551,104,500**
1975	600,000,000			

*Note: This appropriation authority was the continuing resolution. The appropriation amount was the House Allowance, which was the lower of the House or Senate amounts in the first vetoed bill.

**Appropriation after reduction.............................. 530,389,000

Justification

National Cancer Institute

	1974 Base*		1975 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits........	1,838	$35,166,000	1,873	$37,498,000	+35	+$2,332,000
Other expenses........	---	495,223,000	---	562,502,000	---	+67,279,000
Total.......	1,838	530,389,000	1,873	600,000,000	+35	+69,611,000

General Statement

The operational goal of the National Cancer Program is to develop the means to significantly reduce the incidence of cancer in man and morbidity and mortality from cancer, and to ultimately develop the means of eliminating all human cancers. The general strategy of the National Cancer Program is to provide for a balanced program covering the entire spectrum of research, from basic through applied and developmental, by the implementation of laboratory, field and clinical programs that are judged most likely to produce the information and requisite technology that can be transferred rapidly to medical practice.

To achieve the objectives of a nationally coordinated attack on cancer, a National Cancer Program Plan (NCPP) has been formulated with the assistance of 250 of the top cancer researchers in the United States. Seven major objectives have been defined for achieving the conquest of cancer. These objectives cover the full range of activities from prevention of cancer to the rehabilitation of cancer patients. The objectives are formulated in terms of major research areas of cause and prevention, detection and diagnosis, treatment, and cancer biology. These activities are performed through grants, contracts and in-house research.

In the area of cause and prevention, research will continue on the detection of viruses and viral expression in human tumors, the understanding of molecular events in virus-cell interaction leading to malignancy and the application of this information to the control of human cancers. Chemical carcinogenesis research will be expanded to identify and screen potential carcinogens in order to eliminate as many cancer-causing substances from the environment as possible. These efforts will include further development of a series of cell culture systems for more rapid and less costly assay of chemical carcinogens. Improved chemical and immunological techniques will be utilized to an increased degree to detect exposure of human populations to carcinogens and to develop methods to understand and to interrupt the carcinogenic process in man. In addition, epidemiological research studies are performed concerning the frequency and distribution of factors related to the incidence and mortality of cancer and development of preventive measures for cancer in man. Research will continue with the goal of developing models that mimic the human situation or use human tissue cultures for studying specific organ cancers.

*Excludes 1973 appropriation restorations.

In the research area of detection and diagnosis, support is being provided to foster increased research into the use of immunologic methods for the diagnosis of several forms of cancer (e.g., large bowel cancer and leukemia). New studies on the application of such methods as biochemical testing and physical techniques such as ultrasound to cancer diagnosis are being initiated. New efforts have been initiated in the area of automated cytologic diagnosis to facilitate the rapid evaluation of cytologic specimens.

In treatment, more than 40 drugs have been found and are currently in use which can cause regression of some types of clinical cancer. Efforts are continuing to develop additional useful drugs. However, the major research thrust is in combined modality treatment in which drugs are used in combination with other drugs, surgery and/or irradiation to effect tumor regressions. New studies to explore the potential benefit of immunotherapy have been initiated.

A category of cancer biology has been included to reflect that research which cannot reasonably be identified specifically with one research thrust, but which has potential application to them all. This area of basic research accounts for a significant portion of the intramural, collaborative and extramural research programs administered and managed by the Institute.

A major portion of the National Cancer Program is conducted through the specialized and comprehensive cancer centers throughout the country. Planning efforts are generated to insure maximum participation of the physician and the scientific communities. These efforts will assist in the development of community involvement and outreach programs. Efforts to develop an integrated series of centers are underway as a means of assisting in the implementation of the cancer program. Centers cover a broad variety of research and demonstration activities so as to be responsive to the national needs of the Program and also to regional and local needs. The specialized center has particular expertise in a limited number of selected activities (e.g., chemotherapy, radiotherapy). Comprehensive centers have the capability for broad cancer biomedical research, cancer clinical services and investigation, cancer training and education, community programs in cancer diagnosis, and epidemiology and preventive medicine. It is intended that the centers will have the optimal geographical distribution to ensure that the largest possible portion of the population of the country has access to the benefits of cancer research.

Another high priority program is cancer control. The Cancer Control Program was established as a major segment of the National Cancer Program instituted by the National Cancer Act of 1971. Its purpose is to develop, disseminate and aid in the application of existing knowledge which is of immediate value in combating cancer. It is closely coordinated with the research programs of the National Cancer Institute and is developing a close working relationship with other national and international organizations involved in cancer research and the delivery of health care related to cancer. A continuing objective of cancer control is to strengthen and expand the application of cancer knowledge in the practice of medicine and in public health by drawing on all available cancer research findings. The communication of information beneficial to existing or potential cancer patients is being improved through a variety of channels to health professionals and the public.

The management technique of task forces is being utilized at NCI in order to place a greater attack on cancer of specific organ sites of lung, breast, large bowel, prostate and bladder. Cancers of these organ sites represent formidable problems on which relatively little progress has been made. For example, approximately 46,000 of an estimated 75,000 Americans who will be diagnosed this year as having cancer of the colon or of the rectum will die. Included within the cancer research thrusts of the national program are concerted attacks on each of the five major problem sites which have been organized into individual national projects of targeted cancer research. Each of these programs conforms to a comprehensive and detailed long-range plan directed toward improving prevention, detection, diagnosis and treatment of these cancers.

To properly mount and expand the National Cancer Program, adequate manpower and physical facilities are vital. The budget request includes additional in-house NCI personnel to administer and manage large segments of the overall program. The budget includes $22,530,000 for research manpower development needs which are administered through fellowships and training grants, as well as through a new Clinical Education Program. A total of $22,317,000 for construction is being requested for modernization and renovation of cancer centers, to provide better biohazard facilities for research on viruses and chemicals throughout the country, as well as for laboratory and clinical facilities on the NIH campus and at other facilities, including the Frederick Cancer Research Center.

In addition to cancer research supported by the NCI through grants, contracts and intramural activities, significant related activities are being carried out by other Institutes of NIH and other agencies of the Federal, State and local governments, by foundations, associations, volunteer groups and industrial organizations operating with non-Federal funds. Recognizing the desirability of focusing all related efforts on a common goal, the National Cancer Act of 1971 assigned to the Director, NCI, the responsibility of coordinating the overall national effort against cancer and reporting annually on the progress, activities and accomplishments of the National Cancer Program. NCI is expanding its cooperative programs with those of Federal and non-Federal agencies and with private voluntary and professional organizations, as well as in the international sphere.

In accordance with the National Cancer Act, the International Cancer Research Data Bank (ICRDB) was assigned as a responsibility of the Director, NCI. The purpose of this research data bank is to catalog, analyze, and disseminate cancer research information to cancer researchers nationally and internationally. This program will promote and facilitate information exchange between cancer researchers and all physicians. Present information services are now being revised for wider dissemination throughout the world. New services needed by the cancer research community are being identified for development and support within the ICRDB. The NCI plans to utilize fully the services of the National Library of Medicine and other existing information support services and systems nationally and internationally.

DHEW - National Institutes of Health

CROSSWALK - 1974 COLUMN 1975 PRESIDENT'S BUDGET

National Cancer Institute
(In thousands of dollars)

Program	Research Grants			Training Programs		Intramural* Laboratory and Clinical Research	Research and Development Contracts	Other Direct Operations	Cancer Control	Construction	Total
	Regular Program	Specials Cancer Centers	Specials Other	Grants	Fellowships						
1974 Base Obligations											
A. Research Thrust											
1. Cause and prevention research	$15,698	$6,544	$4,288			$18,052	$80,612	$8,287			$133,481
2. Detection and diagnosis research	2,261	10,088	3,580			3,791	13,891	3,638			37,249
3. Treatment research	44,174	29,021	6,986			21,644	62,113	14,736			178,674
4. Cancer biology	42,520	15,851	573			7,177	4,094	7,273			77,488
Subtotal	104,653	61,504	15,427			50,664	160,710	33,934			426,892
B. Resource Development											
1. Cancer centers support		19,211						367			19,578
2. Research manpower development				$12,259	$5,904			367			18,530
3. Construction								307		$30,483	30,790
Subtotal		19,211		12,259	5,904			1,041		30,483	68,898
C. Cancer Control								544	$34,055		34,599
Total NCI 1974 Base Obligations	104,653	80,715	15,427	12,259	5,904	50,664	160,710	35,519	34,055	30,483	530,389

* Includes Collaborative Research and Support.

CROSSWALK - 1974 COLUMN 1975 PRESIDENT'S BUDGET--Continued

Program	Research Grants			Training Programs		Intramural* Laboratory and Clinical Research	Research and Development Contracts	Other Direct Operations	Cancer Control	Construction	Total
		Specials									
	Regular Program	Cancer Centers	Other	Grants	Fellowships						
Unobligated Balance Restored											
A. Research Thrust											
1. Cause and prevention research	$1,571	$745	$334				$9,729				$12,379
2. Detection and diagnosis research	231	47	183				1,534				1,995
3. Treatment research	4,554	3,350	218				7,606				15,728
4. Cancer biology	4,144	2,938	79				790				7,951
Subtotal	10,500	7,080	814				19,659				38,053
B. Resource Development											
1. Cancer centers support											
2. Research manpower development				$4,299	$1,181						5,480
3. Construction										$14,550	14,550
Subtotal				4,299	1,181					14,550	20,030
C. Cancer Control											
Total NCI 1973 Unobligated Balance Restored	10,500	7,080	814	4,299	1,181		19,659			14,550	58,083
Total 1974 Obligations	115,153	87,795	16,241	16,553	7,085	50,664	180,369	35,519	34,055	45,033	588,472

* Includes Collaborative Research and Support.

DHEW - National Institutes of Health

CROSSWALK - 1975 COLUMN 1975 PRESIDENT'S BUDGET

National Cancer Institute
(In thousands of dollars)

Program	Research Grants			Training Programs		Intramural* Laboratory and Clinical Research	Research and Development Contracts	Other Direct Operations	Cancer Control	Construction	Total
		Specials									
	Regular Program	Cancer Centers	Other	Grants	Fellowships						
1975 Estimate											
A. Research Thrust											
1. Cause and prevention research	$17,271	$8,152	$4,913			$19,336	$91,349	$10,641			$151,662
2. Detection and diagnosis research	2,487	11,409	4,085			4,001	15,720	4,042			41,744
3. Treatment research	48,727	36,996	8,432			23,583	68,535	16,855			203,128
4. Cancer biology	46,655	21,195	646			7,560	4,890	8,375			89,321
Subtotal	115,140	77,752	18,076			54,480	180,494	39,913			485,855
B. Resource Development											
1. Cancer centers support		23,082						402			23,484
2. Research manpower development			4,000	6,097	12,066			367			22,530
3. Construction								317		22,000	22,317
Subtotal		23,082	4,000	6,097	12,066			1,086		22,000	68,331
C. Cancer Control								716	45,098		45,814
Total 1975 Obligations	115,140	100,834	22,076	6,097	12,066	54,480	180,494	41,715	45,098	22,000	600,000

* Includes Collaborative Research and Support.

National Cancer Institute

Budget Mechanism

	1974 Base* Number	1974 Base* Amount	1975 Estimate Number	1975 Estimate Amount
Grants				
Regular				
Non-competing....................	1,030	$64,532,000	1,240	$74,512,000
Competing........................	473	40,121,000	533	40,628,000
Renewal......................	(194)	(15,368,000)	(208)	(16,837,000)
New..........................	(279)	(21,474,000)	(325)	(20,265,000)
Supplemental.................		(3,279,000)		(3,526,000)
Subtotal...................	1,503	104,653,000	1,773	115,140,000
Special				
Cancer research centers..........	142	80,715,000	141	100,834,000
Task forces......................	123	10,003,000	114	11,500,000
Research career program..........	76	1,785,000	86	2,000,000
Scientific evaluation............	---	279,000	---	326,000
Clinical education program.......	---	---	67	4,000,000
Radiation development............	3	3,360,000	3	4,250,000
Subtotal.....................	344	96,142,000	411	122,910,000
Total Grants.........................	1,847	200,795,000	2,184	238,050,000
Fellowships				
Non-competing......................	42	454,000	394	5,516,000
Competing..........................	390	5,450,000	536	6,550,000
Renewal..........................				
New..............................	(390)	(5,450,000)	(536)	(6,550,000)
Supplemental.....................				
Subtotal.......................	432	5,904,000	930	12,066,000
Training Grants				
Non-competing......................	169	12,259,000	107	6,097,000
Competing..........................				
Renewal..........................				
New..............................				
Supplemental.....................				
Subtotal.......................	169	12,259,000	107	6,097,000
Intramural Laboratory and Clinical Research..........................		16,265,000		17,127,000
Research and Development Contracts...		160,710,000		180,494,000
Collaborative Research and Support...		34,399,000		37,353,000
Research Management and Program Services..........................		35,519,000		41,715,000
Construction.........................		30,483,000		22,000,000
Cancer Control.......................		34,055,000		45,098,000
TOTAL................................		530,389,000		600,000,000

*Excludes 1973 appropriation restorations.

Research

Authorizing Legislation - Public Health Service Act, Title IV, Part A

	1974 Base*		1975 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits...........	1,763	$33,970,000	1,789	$36,080,000	+26	+2,110,000
Other expenses...........	---	392,922,000	---	449,775,000	---	+56,853,000
Total..........	1,763	426,892,000	1,789	485,855,000	+26	+58,963,000
Subactivities:						
Cause and Prevention Research.............	638	133,481,000	647	151,662,000	+9	+18,181,000
Detection and Diagnosis Research.............	161	37,249,000	168	41,744,000	+7	+4,495,000
Treatment Research.....	647	178,674,000	653	203,128,000	+6	+24,454,000
Cancer Biology.........	317	77,488,000	321	89,321,000	+4	+11,833,000
Total..........	1,763	426,892,000	1,789	485,855,000	+26	+58,963,000
Budget Mechanism:						
Research Grants:						
Regular..............	---	104,653,000	---	115,140,000	---	+10,487,000
Special..............	---	76,931,000	---	95,828,000	---	+18,897,000
Cancer Research Centers..........	(---)	(61,504,000)	(---)	(77,752,000)	(---)	(+16,248,000)
Task Forces........	(---)	(10,003,000)	(---)	(11,500,000)	(---)	(+1,497,000)
Intramural Laboratory and Clinical Research	509	16,265,000	516	17,127,000	+7	+862,000
Research & Development Contracts............	---	160,710,000	---	180,494,000	---	+19,784,000
Collaborative Research & Support..............	894	34,399,000	906	37,353,000	+12	+2,954,000
Research Management & Program Services.....	360	33,934,000	367	39,913,000	+7	+5,979,000
Total..........	1,763	426,892,000	1,789	485,855,000	+26	+58,963,000

The research pursued by the National Cancer Institute can be classified into the areas of cause and prevention research, detection and diagnosis research, treatment research and cancer biology. Research conducted within these areas is pursued in accordance with the objectives and approaches defined in the National Cancer Program Plan. This represents a balanced program covering the entire spectrum of research, from basic through applied and developmental. These activities are performed through grants, contracts and in-house research.

*Excludes 1973 appropriation restorations.

Cause and Prevention Research

	1974 Base*		1975 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Cause and Prevention Research............	638	$133,481,000	647	$151,662,000	+9	+$18,181,000

Cause and prevention research of the National Cancer Program has four major objectives. These objectives are to develop the means: (1) to reduce the effectiveness of cancer producing agents; (2) to modify body mechanisms so as to minimize the hazards of cancer-inducing agents; (3) to prevent transformation of normal cells to cells capable of forming cancers; and (4) to prevent progression of precancerous cells to cancers, the development of cancers from precancerous conditions, and the spread of cancers from primary sites. Research activities directed toward achieving these objectives are conducted and supported by the Divisions of Cancer Research Resources & Centers, Cancer Cause & Prevention, Cancer Biology & Diagnosis, and through the task force mechanism. Research is conducted in collaboration with educational institutions, government agencies, non-profit organizations, and industrial concerns. It is performed throughout the United States and in several foreign countries.

Toward reducing the effectiveness of cancer producing agents, (Objective 1) projects include: assessment of the carcinogenic potential of chemicals, particularly those of environmental significance; search for viruses which cause cancer in man; determination of how viruses associated with human cancers are involved in the formation of these cancers; investigation of smoking habits and modified tobacco products; investigations in co-carcinogenesis and the role of various agents and dietary factors in carcinogenesis; epidemiologic studies on the frequency and distribution of cancer in man; and basic chemical and biological studies contributing to a better understanding of these areas of emphasis.

In minimizing the hazards of cancer-inducing agents, (Objective 2) projects include: efforts to determine why some populations are more susceptible to development of certain cancers than others; studies of chemicals and enzyme mechanisms offering the potential for modifying the effect of industrial and environmental hazards on cancer formation in populations exposed to these hazards; advancement of basic knowledge of how a virus turns a normal cell into a cancer cell; elucidation of the effects of heredity on cancer development; and utilization of any knowledge we have on how cancers form to prevent or reverse this process.

Toward preventing transformation of normal cells to those capable of forming cancers, (Objective 3) projects include: molecular studies on the differences between cancer cells and normal cells, leading to a better understanding of the total cancer process; studies on the properties of cancer viruses and their components; research on the relationship of the tumor virus to the cell in which it grows, in chemical terms; assessment of the interaction of viruses with chemicals and radiation in the formation of cancer; and examination of how the natural defense mechanisms of the host respond to cancer viruses and developing tumors.

Toward developing the means to prevent the progression of cancers, (Objective 4) the approaches and projects include: exploratory efforts to evaluate both

*Excludes 1973 appropriation restorations.

immunological and biochemical methods to induce permanent reversion of malignant cells to the normal state; efforts to identify and eliminate from the environment those factors which cause cancer; research at the molecular level analyzing key factors controlling cell proliferation; and studies to develop new methods of early detection by identifying changes in cell characteristics at the cellular and sub-cellular level.

The 1975 increase of nine positions and $18,181,000 will permit the investigation of significant new research leads as well as the expansion of current studies in the following areas: search for RNA viruses which cause cancer in man; exploration of the role of certain DNA viruses as causative agents of lymphomas and carcinomas, either as carcinogens or co-carcinogens; expanded industrial epidemiology research to include studies for possible effects of air pollution on lung and stomach cancer rates in urban areas; efforts to increase and improve assessment of carcinogenic potential of environmental and industrial chemicals; studies in in vitro and "host-mediated" bioassay of chemical carcinogens; investigation of smoking habits and efforts to develop a less hazardous smoking product; identification of high-risk populations and investigation of correlated dietary and other factors; special collaborative ethnic studies of identified high-risk groups, such as cancer of the nasopharynx in orientals and cancers of the pancreas, esophagus, and liver in blacks; expansion of epidemiologic studies of human breast cancer to determine viral etiology; genetic aspects of cancer causation; application of a laboratory procedure to analyze biochemical, physiological, and morphological variables in populations demonstrating different degrees of susceptibility to cancer development; investigation of the action of carcinogens at the cellular level; research on the immune responses to tumor viruses and to carcinogens; and studies advancing knowledge in molecular and cell biology of the malignant process.

Additional research will also be performed in the following areas: exploration of the differences between normal cells and tumor cells to increase the immunologic defenses of individuals against tumor growth; studies of compounds affecting cellular differentiation and offering potential for modifying carcinogens in some cancers, including possible development of dietary or other means of protecting the host against induction of cancer; data and analytical support of clinical cancer research centers through the Cancer Surveillance Epidemiology and End Results Reporting (SEER) program; and provision of stronger and more flexible computer programming, information systems, resources, and systems analysis support of the etiologic research in the National Cancer Program.

The following are highlights of Cause and Prevention Research accomplishments during the past year:

Virus Cancer Research: (1) Tumor viruses isolated from primates may provide the best probes for detecting the presence of viral information in malignant human cells. (2) Certain herpesviruses have been found to cause cancer in primates. Closely related herpesviruses are commonly found in man and their association with tumors of the head and neck and urogenital tract has been demonstrated. (3) Epstein-Barr virus, which is associated with Burkitt's lymphoma and mononucleosis, was shown to cause cancer in primates. This provides an important animal model for studying these human diseases. (4) Preliminary evidence indicates that herpesvirus-associated cancer may be detectable at very early stages through an antibody found in the blood. (5) New methods have been developed for converting viruses from the dormant to the active state. This provides a new way of looking for hitherto undetectable human tumor viruses. (6) Rapid and sensitive biochemical tests have been developed for detecting virus activity in cancerous cells. Emphasis is being placed on large-scale application of these techniques to screen human populations at high risk to cancers, such as breast cancer. (7) Animal model systems indicate that a viral vaccine can reduce the incidence of spontaneous tumors. (8) Biochemical tests have shown that the hereditary material of some animal cancer viruses is similar to the hereditary material in human tumors. This indicates that these human tumors may contain viral information. (9) Purified and concentrated viruses and viral reagents were provided to over one hundred collaborating laboratories throughout the world, and NCI Virus Program repositories processed over 50,000 individual items. (10) Efforts of NCI and contract scientists were combined to determine quickly that four candidate human cancer viruses were actually of non-human origin. (11) A virus resembling RNA tumor virus has been found in a high percentage of baboon placentas and in some human placentas. The implications of this new finding are receiving intensive study.

Carcinogenesis Research: (1) The number of potentially carcinogenic chemicals under test in animals is about 450 and includes many of industrial and environmental significance. (2) Progress has been made in developing and optimizing assays using cell cultures instead of animals for testing and screening potential carcinogens; availability of the new assays will permit a tenfold increase in the number of chemicals under test. (3) Tobacco research to develop a less hazardous cigarette has been expanded with concentration on selecting tobaccos, production, and machine smoking of approximately 40 types of cigarettes. Analysis and bioassay of smoke condensates indicates that a decrease in tumorigenicity can be obtained by manipulating various processes and components. (4) Research in the lung cancer program has developed methods which permit one to study morphologic changes and biochemical events directly on respiratory epithelium in animals and human tissues. (5) Continuing studies are yielding information on the influence of diet and associated microbial metabolism on colon cancer. (6) A major new effort has been initiated to study carcinogen metabolism and toxicology which offers a potential route for altering the carcinogenic process, possibly even after exposure. Initial efforts are concentrated on studying nitrosamines, an extremely potentially hazardous group of carcinogenic compounds. (7) In the area of immunology, antibodies to carcinogens have been produced. Vaccines and cell wall substances from a microorganism, Bacillus Colmette Guerin (BCG), continue to be studied and show potential value as prophylactic or therapeutic agents. (8) An active and important collaboration has been established with other governmental agencies, including the Food and Drug Administration, the Environmental Protection Agency, the National Institute for Occupational Safety and Health, the Atomic Energy Commission, the United States Department of Agriculture, the Department of Labor, the Department of Defense, and the National Aeronautics and Space Administration.

Field Studies & Statistics: (1) For the first time, cancer mortality in the U.S. can be shown on a county level, with excesses indicating suspected environmental exposures. (2) Studies identified an increased risk of cancer among recipients of kidney transplants. (3) Our staff initiated an international survey of childhood cancer and discovered variations in the patterns of occurrence of certain cancers that suggest the importance of environmental factors. (4) Data collection and processing have been completed in the Third National Cancer Survey. This survey enumerates all cancer diagnosed during the 3-year period 1969-1971 in different areas of the United States, with a combined population of 20 million people. (5) A continuing program of data collection has been organized in nine geographic areas. This is known as the Cancer Surveillance, Epidemiology, and End Results Reporting (SEER) program. This program is designed to provide information on trends in cancer incidence, variation among different population groups and geographic areas, changes in diagnostic and treatment practices and associated end results. (6) It was discovered that high beef consumption might possibly be related to cancer of the large intestine in Japanese immigrants and Japanese descent Americans as opposed to rates in Japan.

The Frederick Cancer Research Center has established large-scale production of oncogenic viruses which are provided throughout the country to researchers trying to determine what role viruses may play in human cancer. In addition to basic research, viral oncology efforts include development of improved methods for production of viruses and other reagents and preparation of special viral diagnostic reagents. The carcinogenesis program includes: initiation of large-scale bioassay with a target of 50 to 60 chemicals under test by the end of FY 1974, a major analytical capability which includes studies in the metabolism and mechanism of action of specific carcinogenic substances and studies in *in vitro* and "host-mediated" bioassay methodologies. Both of these programs also have initiated biohazard control efforts. Hundreds of thousands of animals have been produced and supplied for experiments at the Center and throughout the National Cancer Program. An advanced systems laboratory, responsive to the needs of new research findings, has been established to offer the most modern facilities to visiting scientists from all over the world.

Detection and Diagnosis Research

	1974 Base*		1975 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Detection and Diagnosis Research...	161	$37,249,000	168	$41,744,000	+7	+$4,495,000

The goals of detection and diagnosis research, described in Objective 5 of the National Cancer Program Plan, are to develop the means to achieve an accurate assessment of (a) the risk of developing cancer in groups and individuals and (b) the presence, extent and probable course of existing cancers. Seven general approaches to these goals are identified in the Plan, and these can be grouped into three areas; detection, diagnosis and prognosis. Detection includes the identification of population groups with high risk of cancer (approach 5.1); the identification of conditions associated with cancer (approach 5.2); the development of procedures for screening population groups for cancer (approach 5.3); and the prediction of individuals who will get cancer (approach 5.5). Diagnosis research is the improvement of procedures to determine the presence and location of cancer in individuals (approach 5.4). Prognosis is the determination of cancer characteristics that cause different growth rates and probability of spread to predict the course of cancer in individuals (approach 5.6). The public use of prevention, screening and detection methods (approach 5.7) is part of the Cancer Control Program.

Detection. Demographic studies in the Cancer Surveillance, Epidemiology and End Results (SEER) program identify population groups for whom detection methods need development and application. Much effort is devoted to research in cancer cytology, which has already been most productively used in screening for cervical cancer (Pap test). This includes work to understand the biological significance of the many abnormal, but not cancerous, cells in such specimens, but the major effort is directed to wider application and to simplification of methods. Several large projects are applying routine cytologic screening to sputum from heavy smokers as a means to improve survival through early detection of lung cancer in this high risk group. Since wider application of cytologic screening for cervical cancer, and extension of screening to groups at risk of lung cancer, bladder cancer and perhaps cancer of other organs, will vastly increase the number of these tests to be done, a major program has been started to develop machines to assist the pathologist in reading these specimens. Prototype machines have been made which use a laser beam and supporting electronics to separate normal cells from those suspicious of cancer. With these machines it may be possible to discard the bulk of completely normal tests and let the technicians concentrate on the suspicious ones. In other detection modalities, the value of mammography in breast cancer screening has been proven. Also the relative value of the simpler technique of thermography is under evaluation.

Another area of research toward cancer detection (and diagnosis as well) is in the field of immunology. Tumor cells have on their surfaces specific antigens, molecular groupings of protein and carbohydrate, that are not detected on normal cells. Sometimes these antigens are freed from the cell and circulate in the blood; the body may form circulating antibodies or sensitized cells that

*Excludes 1973 appropriation restorations.

react with tumor antigens. Thus, given the extreme sensitivity of immune reactions, if the tumor antigen can be purified it should be possible to devise highly sensitive and specific diagnostic tests for tumors that can be used on blood samples. Accordingly, a great deal of research is in progress to isolate specific tumor antigens, and to work out methods for their assay. To date, the most useful immunodiagnostic tests are based on circulating tumor products, such as carcinoembryonic antigen (CEA) and alpha fetoprotein. Clinical testing shows these reactions are of only limited use in early diagnosis, although they are valuable in following response to treatment. Rapid evaluation of new candidate tests has been made simpler by the establishment of banks of serum specimens from patients with various types and stages of cancer. The possibility that tests of cell-mediated immunity may have useful applications in diagnosis is being explored.

Diagnosis. This program seeks ways to tell if cancer is present or not in a single patient, and exactly where it is. The effort in immunology research on identification of tumor antigens has the goal of identifying individuals with a tumor, as well as identifying those who possibly have or may develop cancer. With the progress expected in tumor immunology it is believed that some antigens, e.g., cancer virus antigens, will be found that indicate a predisposition to cancer, but that others, e.g., tumor specific antigens, will not appear until cancer is actually present. The localization of cancer in a patient is quite a different problem. The great value of flexible fiberoptic endoscopes in tumor localization has been proven, especially in bowel and lung cancer. With these instruments, small tumors invisible by x-ray can be found anywhere in the large bowel and in a large part of the bronchial tree, at a stage when surgery should cure them. Broad application of these techniques and of other diagnostic methods which have been proven in controlled clinical trials is being encouraged as part of the cancer centers program.

Prognosis. Research in the growth and spread of tumors is closely involved with research in treatment. Some immunodiagnostic tests, or markers, are valuable guides to treatment. Also included here is immunologic research on how the body's normal defense against foreign cells is deranged in cancer, allowing tumor growth. A recent exciting finding under intensive study is the demonstration of the "tumor angiogenesis factor," a substance produced by experimental tumors that promotes the growth of blood vessels into them, permitting growth beyond just a tiny nodule.

Some tumors secrete biochemical substances such as hormones into the blood stream. As some of these markers, e.g., human chorionic gonadotropic hormone (HCG), have already proven valuable as prognostic markers, it seems likely that many more of them can be developed. Another area of study in tumor growth is the effect of normal hormone excretion. Many cases of widespread breast cancer respond partially to ovariectomy. An understanding of why this happens should help to predict which women will respond to the operation, and should also lead to better non-surgical treatment. Application of these and other research results, and of more exact pathological staging of cancer, is being fostered in the cancer centers program.

The 1975 increase of seven positions and $4,495,000 will be used for efforts with a high probability of success in reducing cancer mortality through early detection and diagnosis. In cancer detection development of automated equipment for cancer cytology will continue, centering on the preparation of specimens for existing prototype equipment. Additional effort will be devoted to identifying tumor antigens, and to developing immunologic tests for these antigens. Also, work in identifying hormones produced by tumors will be studied, for use in screening, in diagnosis and in following the results of treatment. Work will start on a specific test for human blood in the feces; this will provide a simple screening method for bowel cancer. New x-ray equipment for cancer diagnosis, such as computer assisted tomography, will be quickly evaluated, and further equipment development will be undertaken. In all aspects of cancer diagnosis and prognosis, there will be broad application of new and existing methods through the cancer centers program.

The following are highlights of Detection and Diagnosis Research accomplishments during the past year:

A very real improvement in the mortality of cancer of the lung now appears possible through early detection by regular cytologic examination of sputum. In a long term study of symptom-free middle aged male cigarette smokers, cells suspicious of cancer have been found in a year's time in nearly one percent of those tested.

This same study of men at high risk of lung cancer has provided a major diagnostic advance. Finding cells suspicious of cancer in the sputum cannot tell where the disease is in the lung, nor are small surgically curable cancers visible on x-ray. However, with the flexible fiberoptic bronchoscope it has been possible to find almost every such cancer when present, and pinpoint it to guide the surgeon.

A milestone has been reached on the road toward automation of cytologic screening for cancer with the completion of a prototype instrument to separate normal cells from cells suspicious of cancer in a suspension flowing past a laser beam. Further development will be needed after testing in the laboratory and clinic, but the instrument has the potential of vastly increasing the screening test output of medical personnel.

The first immunodiagnostic test for cancer has become available to the general medical profession with the licensing by the FDA of a radioimmunoassay for carcinoembryonic antigen (CEA). It may be valuable for following response to treatment, especially in cancer of the bowel, although it cannot be used for cancer screening. Two more radioimmunoassays, for alpha fetoprotein (AFP) and human chorionic gonadotropin (HCG) have shown great value in a research setting for the diagnosis of testicular tumors, and for guiding treatment. The transfer to patients of results of basic research in cell immunity has begun with the finding that the proportion of one type of circulating immune cell (T-lymphocyte) is reduced in patients with cancer.

Treatment Research

	1974 Base*		1975 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Treatment Research.....	647	$178,674,000	653	$203,128,000	+6	+$24,454,000

The national program for research in treatment of patients with cancer is encompassed within Objective 6 of the National Cancer Plan, the goal of which is to "develop the means to cure as many patients as possible and to maintain maximum control of the cancerous process in patients not cured." This objective encompasses approaches which include: development and application of therapy (approach 6.1); acquisition of antitumor drugs (approach 6.2); reversion of the neoplastic process (approach 6.3); beneficial enhancement of the immune mechanism (approach 6.4); dissemination of research information related to advances in treatment (approach 6.5); and development of an epidemiology of treatment (identification of individuals likely to benefit from specific types of therapy) (approach 6.6).

The National Cancer Institute serves as the focal point for research in cancer treatment in this country and probably the world. Prior to the last decade, surgery and radiotherapy were the only modalities of therapy which could effect cures in patients with cancer. However, beginning with the demonstration in the 1960's that women with choriocarcinoma could be given a normal life expectancy with the use of antitumor drugs alone, continued drug research and development conducted largely under the sponsorship of the Institute has improved prognosis in at least nine other forms of cancer. In two of these types, choriocarcinoma and Burkitt's lymphoma, cures are achieved in a majority of patients. In other cancers (acute lymphocytic leukemia, Hodgkin's disease, rhabdomyosarcoma, testicular tumors, Wilms' tumor, Ewing's tumor, retinoblastoma, and histiocytic lymphomas) combinations of drugs or drugs combined with surgery or radiotherapy can result in a normal life expectancy in significant numbers of patients. These tumors are in general, rapidly growing, normally not localized and have a high proportion of cells in multiplication. The experience and knowledge gained from advances in the management of these rapidly growing tumors are now being applied to the more common slowly growing tumors that are localized at first but disseminated later in the course of the disease and have a small proportion of cells in division. In an increasing number of these types of cancers, remissions are being achieved and prognosis for survival is being improved. Included in this latter group are adenocarcinoma of the ovary and the breast. In other cancers such as lung cancer and bowel cancer, significant tumor regressions can be obtained in a sizeable percentage of patients although prognosis for survival has not yet been improved.

The 1975 increase of six positions and $24,454,000 will be devoted to the application of all available knowledge and experience in therapy to the management of patients with the slowly growing more common tumors since they account for 70-80% of all cancer deaths. All modalities of therapy will be pursued to strive for maximum effectiveness. However, since combinations of modalities have proven superior to agents used alone in disseminated disease, greater emphasis will be placed on research in both animal tumor systems and in patients in order to identify optimal combinations.

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*Excludes 1973 appropriation restorations.

The majority of patients having malignant solid tumors (such as those of the breast, lung and bowel) already have disseminated disease when first seen by the physician. This is true even when the usual diagnostic tests seem to indicate that the disease is still localized. Patients with truly localized disease are often cured by radiotherapy or surgery. However, in many patients with early disease and in all patients with disseminated disease, therapy must be directed at both the local tumor and the diffuse disease. Chemotherapy can destroy malignant cells anywhere in the body and is the treatment of choice at the present time for the management of disseminated disease although immunotherapy seems to hold great promise for the future. The use of surgery and/or radiotherapy with chemotherapy and/or immunotherapy combine local and disseminated cell kill which may lead to the eradication of all cancer cells in a high percentage of cases.

The major effort in the search for drugs in this country and abroad will be in identifying agents with activity against slowly growing tumors and on combinations of these drugs with other modalities of therapy. New animal screens simulating the biology of slowly growing tumors, and biochemical and cell culture screens have been added to take advantage of recent advances in our knowledge of molecular events associated with malignant change. The number of materials screened for antitumor activity will reach approximately 50,000 per year but more selective criteria will be utilized in the initial testing and the selection for further testing of those compounds with the best chance of affecting slowly growing tumors.

A major reason for lack of drug response is failure of the drug to reach its target, consequently, there will be intensive efforts to investigate the pharmacologic disposition of antitumor drugs. For the optimal use of a drug, pharmacologic studies should be performed in every patient during the course of treatment. Several such programs are now supported and this activity will be expanded in 1975. Another problem results from the fact that present day techniques such as x-rays are too insensitive to enable the clinician to determine whether treatment has rid the body of all tumor cells. In order to assess rapidly the curative capacity of systemic therapy, particularly of combination therapy, a method of estimating the number of tumor cells in the body after each course of therapy is essential. There are now a number of promising leads in developing such methods for several tumors and efforts in this area will be expanded. The recent rapid advances in knowledge concerning reverse transcriptase in animal tumors and in the acute leukemias and breast cancer have led to the expansion of these studies with emphasis on drug inhibitors of this key enzyme, and this area will continue to be emphasized.

The biggest time loss in evaluation of combination therapy results from inadequate clinical resources for Phase II (therapeutic effectiveness) studies. Extensive efforts for expansion are under way, supported by contracts and grants (cooperative groups and organ site programs) and by increasingly active liaison with other groups in the U.S. and abroad. Such studies are already under way in brain tumors, lung, breast, colon, ovarian, and testicular cancers. In 1975, cancer of the cervix, prostate, pancreas, and bladder will be included. Phase III studies comparing various remedies are under way in breast cancer, lung cancer, lymphomas, testicular tumors, ovarian cancer and colon cancer. These are being conducted in-house, under contract, and in the grant-supported Clinical Trials Program which includes 22 groups composed of 1600 investigators. In 1975, such studies will be expanded to include head and neck, bladder and prostate cancer.

Programs in laboratory and clinical research on the use of BCG and other enhancers of the immune mechanism are under way, but these efforts will receive particular emphasis in 1975. It is planned that large scale programs to evaluate the usefulness of these materials in several different human tumors will be undertaken in 1975.

Research into the application of high LET radiation including neutrons and negative pi mesons, for use in cancer patients will be expanded. Development of new techniques for localization and delineation of deep seated tumors utilizing diagnostic x-rays and radioisotopes will be pursued.

The following are highlights of Treatment Research accomplishments during the past year:

Use of combination drug treatment produced complete remissions in 45% of patients treated for advanced non-Hodgkin's lymphoma.

Surgery followed by radiotherapy has increased the rate of five-year survival in women with advanced cancer of the lining of the uterus.

Drug treatment combined with radiotherapy has produced temporary objective tumor shrinkage and improvement in patients with small cell carcinoma of the lung, usually the most aggressive lung tumor.

Streptozotocin (an antibiotic drug) has produced measurable responses in 50% of patients with islet cell carcinoma of the pancreas.

Megavoltage radiation generated by the Stanford linear accelerator has permitted 72% of patients with cancer of the prostate gland to survive at least 10 years.

Deaths from infection among patients with acute leukemia have been reduced through the use of protective environments and antibiotic therapy.

A total of 47,429 new materials were submitted for animal testing for anticancer activity in 1973. Fifteen others have been approved for study against human cancer. A "mini-screen" system requiring significantly smaller quantities of materials and animals has been developed by NCI to expedite the screening of chemical agents or potential anticancer drugs.

Lung cancer is the most common lethal tumor in the United States and is a type of cancer in which the combined modality approach is highly appropriate. Surgery has been the most common single agent employed in the initial management of patients with this cancer but overall five-year survival has remained in the range of 8 to 10%. Radiation therapy and chemotherapy alone have not led to significant improvements in either the incidence of remissions or their duration. However, recent experience in at least one type of lung cancer, oat cell carcinoma, permits some degree of cautious optimism that with the use of combinations of modalities, prognosis and survival will improve. In this type of lung cancer, considered to be the most virulent and aggressive, a combination of chemotherapy and radiation therapy resulted in a high incidence of response in a relatively small series of patients.

Another approach which appears to have important implications is therapy with high linear energy transfer (LET) radiation such as neutrons, pions and heavy ions. At the present time, four studies - three neutron and one pion - are being funded which may ultimately lead to randomized clinical trials. By the end of 1974, all four will be engaged in preliminary work on humans.

The treatment of cancer by the use of immunologic processes (immunotherapy) continues to be an exciting field with increasing evidence in animals that the immune system can indeed destroy tumors. One promising lead has indicated that substances which are strong stimulators of immune system activity can effectively stimulate immune activity against established cancers. In certain instances complete destruction of localized cancers can be achieved.

Cancer Biology

	1974 Base*		1975 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Cancer Biology......	317	$77,488,000	321	$89,321,000	+4	+$11,833,000

Cancer Biology is an area of research which provides fundamental information on the causes and nature of cancer in man, with the expectation that this will result in better methods of prevention, detection and diagnosis, and treatment of neoplastic diseases. It includes, therefore, research that cannot reasonably be classified in any of the specific research thrusts but where results have potential application to all thrusts.

The 1975 increases of four positions and $11,833,000 will permit the initiation of important new studies in cell hybridization, cell suppression and reversal of malignant cell growths. Such studies will have direct bearing on the understanding of the cancerous process as it ultimately relates to patient treatment.

In order to test the feasibility and potential effectiveness of pion and heavy ion radiation therapy on human subjects, extensive studies involving associated radiation biology and physics must be initiated.

Other work to be done includes new procedures to isolate pure cultures of mammalian cells, including tumor cells, and maintain them in a stable state. Methods are being developed for mass cultures of lymphocytes for possible therapy, and of neoplastic cells for the preparation of specific antigens, since they have potential for the prevention and therapy of cancer.

Tumor associated antigens induce in the host the production of both humoral and cell bound antibodies. Each of these types of antibody will be studied extensively in order to understand the basic phenomena involved in diagnosis, prevention and treatment of neoplasia. Additional studies will be explored on a tumor angiogenesis factor (TAF) which appears to be necessary for the understanding of tumor growth.

Efforts will be focused on the characteristic biochemistry of the cancer cell and the influence of cancer on the biochemistry of the host. This is necessary in order to study the mechanisms by which cells produce and control their energy, the biosynthesis, transport, mode of action, and catabolism of steroids, the regulation of protein synthesis and the use of physical methods to identify cells.

Additional emphasis will be placed on studying the transfer of genetic instructions from DNA to messenger RNA to proteins, and on the built-in controls of these processes.

Studies of biochemical and physiological differences between normal and cancer cells and between normal animals and those bearing tumors will be continued to determine which differences are significant to the malignant state and what can be done to inhibit or reverse these changes.

The following are highlights of Cancer Biology accomplishments during the past year:

Analysis of malignancy by fusing isolated cancer cells with one another or with normal cells has revealed properties of cancer cells which can be exploited to suppress or reverse malignancy. These exciting findings suggest the desirability of developing another approach, the goal of which would be to induce cancer cells to revert to normal growth and behavior, rather than to attempt to destroy the errant cells, often at great risk to the host.

Considerable progress has been made in enhancing various components of the immune system in cancer patients, causing the tumors to be at least partially destroyed in much the same manner as bacteria are destroyed in ordinary infections. The complexity of the immune system and the fact that tumors are not "foreign" tissue, require that much basic work be done before host immunity can be used to inhibit human cancer development.

Progress in determining the portion of the nuclear DNA responsible for continuous gene repression has been encouraging. The precise molecular nature of this type of repression is now being carried out in test tube studies with purified components which permit analyses of cell component interactions and activities. The molecular workings of the cell can now be probed to analyze the events leading to the failure of growth repression which characterizes cancer cells.

During the past year several chemicals have been isolated which can be used to alter cell behavior in tissue culture. By changing the chemical environment in which the cells are grown, normal cells were made to assume the growth pattern of cancer cells, or cancer cells can be made to behave normally. Methods for inducing permanent changes in cell behavior are being developed which will effect these changes in living animals and humans as well as in tissue culture.

Resource Development

Authorizing Legislation - Public Health Service Act, Title IV, Part A

	1974 Base*		1975 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits..........	31	$531,000	33	$601,000	+2	+$70,000
Other expenses..........	---	68,367,000	---	67,730,000	---	-637,000
Total.........	31	68,898,000	33	68,331,000	+2	-567,000
Subactivities:						
Cancer Centers Support.............	12	19,578,000	14	23,484,000	+2	+3,906,000
Research Manpower Development.........	8	18,530,000	8	22,530,000	---	+4,000,000
Construction..........	11	30,790,000	11	22,317,000	---	-8,473,000
Total.........	31	68,898,000	33	68,331,000	+2	-567,000
Budget Mechanism:						
Research Grants:......	---	19,211,000	---	27,082,000		+7,871,000
Special............	(---)	(19,211,000)	(---)	(27,082,000)		(+7,871,000)
Fellowships...........	---	5,904,000	---	12,066,000		+6,162,000
Training Grants.......	---	12,259,000	---	6,097,000		-6,162,000
Research Management & Program Services....	31	1,041,000	33	1,086,000	+2	+45,000
Construction..........	---	30,483,000	---	22,000,000		-8,483,000
Grants..............	(---)	(23,550,000)	(---)	(17,000,000)		(-6,550,000)
Contracts...........	(---)	(6,933,000)	(---)	(5,000,000)		(-1,933,000)
Total.........	31	68,898,000	33	68,331,000	+2	-567,000

In augmenting the research conducted by the Institute, this area contains Cancer Centers Support, Research Manpower Development and Construction. The Cancer Centers Support program is designed to: determine the feasibility of establishing new centers; generate planning efforts to ensure maximum participation of the medical community served by the centers; help support administrative activities of the center; and provide funds for developing new programs within the center. The Research Manpower Development area supports research training and education in scientific fields related to cancer research. Construction monies provide the resources required for the modernization and renovation of existing space for cancer laboratory and clinical research purposes.

Cancer Centers Support

	1974 Base*		1975 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Cancer Centers Support..............	12	$19,578,000	14	$23,484,000	+2	+$3,906,000

The Cancer Centers Support Activity pertains to Exploratory Projects and Core Grants only. The dollars for research performed at cancer centers are reflected under the appropriate research areas of cause and prevention, detection and diagnosis, treatment and cancer biology.

Exploratory Projects are designed to determine the feasibility of establishing specialized and comprehensive centers and to generate the planning efforts essential to ensure maximum participation of the physician and scientific communities. Moreover, they will provide plans to develop community involvement and outreach programs.

Core Grants are used to support the administration, common services and collaborative activities of cancer centers and to provide "seed money" for development of new programs within the centers. The core grants provide only a small part of the operational costs; the remainder of the operational costs are supplied through individual research grants, center grants, contracts, and non-federal sources.

In 1975, feasibility studies will be encouraged with emphasis on expansion of existing facilities. Community impact studies will be initiated to maintain local visibility and encourage institutional and community cooperation. It is expected that these efforts will culminate in the establishment of area councils in key cities where optimal communication and cooperation is being sought.

In 1975, continued emphasis will be placed on the "core" support mechanism as opposed to large "umbrella" grants. Core support provides the director of a cancer center with an operating budget and thus enables him to establish coordination between the individual institutions and departments participating in a Centers program.

Comprehensive cancer centers are established to conduct long term multidisciplinary programs related to cancer. The ultimate objective of these programs is to establish a nationwide system of comprehensive centers which engage in basic and clinical research, improve diagnosis and treatment of patients, train an effective cancer cadre for the future, and influence the standard of cancer care in the surrounding areas.

Currently, the NCI has recognized 12 comprehensive cancer centers as follows:

The Fred Hutchinson Cancer Research Center affiliated with the University of Washington in Seattle; the University of Southern California, Los Angeles; the University of Alabama at Birmingham; the University of Wisconsin, Madison; the University of Miami in Florida; Duke University in Durham, North Carolina; Johns Hopkins University, Baltimore, Maryland; Children's Cancer Research Foundation in Boston, Massachusetts; and the Mayo Foundation in Rochester, Minnesota. These centers have been identified as comprehensive centers in addition to the three centers which were judged to be comprehensive at the time of the National Cancer Act of 1971: Roswell Park Memorial Hospital in Buffalo, New York; Sloan-Kettering

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*Excludes 1973 appropriation restorations.

Institute and Memorial Hospital in New York City; and the M.D. Anderson Hospital and Tumor Institute in Houston, Texas.

By the end of 1974, it is expected that six additional comprehensive cancer centers will be recognized by NCI to a new total of 18. Planning is now underway in many areas throughout the country to determine the feasibility of establishing new comprehensive cancer centers.

In addition to the comprehensive cancer centers, NCI supports 49 specialized cancer research centers which make the latest cancer research advances more widely available to physicians and patients. These centers cover a broad range of techniques with some having major emphasis in areas of basic research relevant to the cancer problems, to others with major emphasis on clinical aspects of the cancer problems. There is still an urgent need to establish additional new programs, particularly in areas where promising new leads need clinical testing and application, in gap areas where little work is being done, and in relatively new fields such as immunology.

The Cancer Centers Program is evolving into a geographically balanced combination of specialized and comprehensive cancer centers providing a broad base for research, demonstration of the latest and best techniques of diagnosis and treatment, and community outreach.

Research Manpower Development

	1974 Base*		1975 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Research Manpower Development..........	8	$18,530,000	8	$22,530,000	---	+$4,000,000

Research Manpower Development represents several training programs, and a new Clinical Education Program. The various programs involved consist of the following:

a. Clinical Training. Grants awarded to medical, dental and osteopathy schools, to advance the caliber of education in cancer-related subjects.

b. Graduate Research Training. Predoctoral and postdoctoral training awards to institutions in various scientific disciplines to provide a source of competent research manpower.

c. Fellowships. Awarded to qualified American citizens for postdoctoral research training to be obtained in this country or abroad, in basic and clinical sciences.

d. Clinical Education Program. Awards to educational institutions in order to create more innovative teaching programs related to cancer.

With the release of 1973 funds, those fellowships and training grants previously phased out, are now being restored, and will be renewed in accordance with the project period of the grant awards. The newly established NIH Manpower Development Program for postdoctoral individual research fellowships and institutional research fellowships will be utilized to the maximum extent possible.

The 1975 requested funds of $22,530,000 include $18,530,000 for fellowships and training grants, and $4,000,000 for the new Clinical Education Program. Since physicians and dentists are normally the first medical people to suspect or diagnose cancer, their education is thus of major importance to the National Cancer Program. Grants will be awarded to schools of medicine, dentistry and osteopathy, cancer institutes and major teaching hospitals. No funds will be provided for stipendiary support under the Clinical Education Program.

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*Excludes 1973 appropriation restorations.

Construction

	1974 Base*		1975 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Construction.........	11	$30,790,000	11	$22,317,000	---	-$8,473,000

Within the provisions of the National Cancer Act of 1971, construction authority was provided to the National Cancer Institute. The intent of the program is to create additional facilities as well as to improve existing facilities essential to the expanding cancer program. The National Cancer Institute pays up to 75% of the cost of construction in connection with cancer research centers.

1975 funds totalling $22,317,000 are requested for construction in connection with modernization and renovation of cancer research centers, biohazard facilities, and NIH and other research facilities including the Frederick Cancer Research Center.

At the June 1973 meeting of the National Cancer Advisory Board, it was recommended that construction funds be included in the 1975 budget in support of upgrading and development of biohazard facilities at institutions throughout the country where research is conducted on viruses and chemical compounds related to cancer. A limited amount of the total requested funds will be used for modernization and renovation of biohazard facilities.

The construction funds are essential to the strengthening of research programs, particularly at cancer centers, by aiding in the development of new, high quality multidisciplinary cancer research efforts in regions of the country where they do not now exist. Funds will be used to improve clinical research space and laboratories relating to such activities as chemotherapy, radiation therapy, immunology, cell and molecular biology, virology, and carcinogenesis.

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*Excludes 1973 appropriation restorations.

Cancer Control

Authorizing Legislation - Public Health Service Act, Title IV, Part A

	1974 Base*		1975 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits.........	44	$665,000	51	$817,000	+7	+$152,000
Other expenses.........	---	33,934,000	---	44,997,000	---	+11,063,000
Total........	44	34,599,000	51	45,814,000	+7	+11,215,000
Budget Mechanism:						
Research Management & Program Services...	14	544,000	16	716,000	+2	+172,000
Cancer Control.......	30	34,055,000	35	45,098,000	+5	+11,043,000
In-house...........	(30)	(1,055,000)	(35)	(1,275,000)	(+5)	(+220,000)
Contracts..........	(---)	(26,000,000)	(---)	(34,423,000)	(---)	(+8,423,000)
Grants.............	(---)	(7,000,000)	(---)	(9,400,000)	(---)	(+2,400,000)
Total........	44	34,599,000	51	45,814,000	+7	+11,215,000

The goal of the Cancer Control Program is the rapid and effective application of present research knowledge in order to prevent the occurrence of cancer, minimize its impact, and reduce the number of cancer deaths. In order to achieve this goal, three separate objectives have been established: (1) communication of successful findings to the professional and lay public for direct application to present and potential cancer victims; (2) motivation of the professional and lay public to act on the findings; and (3) research on the most effective organization of cancer-related medical services; on the present quality, use, and availability of medical care; on improved ways to communicate present knowledge; and on factors that cause people to accept, or reject, changes that would reduce illness and deaths from cancer.

Cancer Control Program efforts are aligned with the major objectives of the National Cancer Plan. It should be noted, however, that the research support provided in this program will be specifically related to demonstrating the effectiveness of research leads, and to improving the application of cancer control measures deemed ready for widespread use.

Cancer Control is divided into three major program components: Prevention, Early Detection, and Diagnosis and Treatment (including Rehabilitation and continuing care).

The specific objectives of Prevention are to: (1) obtain an understanding and acceptance among people (as individuals or in groups) of what cancer is, and of steps they can take to reduce the risk of cancer; (2) motivate people (as individuals or in groups) to take these steps; and (3) develop new educational materials and delivery procedures appropriate to accomplish these objectives.

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*Excludes 1973 appropriation restorations.

The primary goals of Early Detection are to: (1) develop practical programs to increase frequency of early detection of cancers by the demonstration of efficient screening methods and (2) provide motivation to use these methods.

The goals of Diagnosis and Treatment are to: (1) develop and establish procedures throughout the country whereby the best available diagnosis and treatment methods will be brought to bear on controlling the cancerous process in all patients in order to effect as many cures as possible and/or to minimize the effects of the disease and its treatment on the patient; and (2) improve the quality of cancer patient care through improved rehabilitation techniques and devices, and continuing care. To reach these goals, this area must be developed in concert with a variety of public and private agencies.

Supporting these three components are activities in Education and Training, and Program Management and Evaluation.

The 1975 increase of seven positions and $11,215,000 will be used in support of program plans described below:

Prevention. The requested increase of $942,000 to a 1975 level of $3,207,000 will allow new projects to be initiated in environmental hazards (i.e., food additives, industrial effluents, etc.). Present planning in the control of cancer-related occupational hazards will permit initiation of projects in early 1975. These new activities will be in close collaboration with a variety of agencies and organizations outside the Federal government, as well as other Federal agencies. Selected projects directed toward the reduction of lung cancer, the Nation's No. 1 cancer killer among men, will be supported and managed jointly with the National Clearinghouse for Smoking and Health.

Early Detection. The requested increase of $3,975,000 to a 1975 level of $16,951,000 will support: (1) programs in provider (health profession) and consumer (public) motivation; (2) planned expansion of projects involving established procedures for the early detection of cancer; (3) the evaluation of the general applicability of new procedures; (4) identification of populations at special risk in which specific early detection tests will have highest priority; and (5) development of administrative and logistic procedures particularly applicable to cooperative efforts between the National Cancer Institute, State and local health departments, professional societies, private sector, and other Federal agencies. During the period of 1974 to 1976, there is special emphasis in the early detection of breast and cervical cancer.

Diagnosis and Treatment. The requested increase of $6,298,000 to a 1975 level of $25,656,000 will be directed toward developing, initiating and supporting additional projects in four areas: (1) more effective communication with physicians, other health professionals and the general public about cancer diagnosis and treatment; (2) provision of optimal cancer treatment (including continuing care) through existing community resources and mechanisms; (3) improved access to consultative services throughout the country; and (4) additional high-priority areas of rehabilitation.

The following are highlights of Cancer Control accomplishments during the past year:

A detailed long-range plan has been drafted, operating procedures settled, staff recruited, and advisory mechanisms established. Close working arrangements now exist with other Federal agencies and other groups concerned with cancer, including State health offices, the National Clearinghouse for Smoking and Health, the American Cancer Society, and several medical specialty associations. A detailed national survey and analysis of present cancer programs in State organizations is nearly complete.

One of the first program efforts, now in full operation, was the establishment of seven networks of hospitals to improve the treatment of childhood leukemia and of Hodgkin's Disease and lymphomas at all ages. Until recently these diseases were almost uniformly fatal. Curative treatment is now possible in many cases, but it is very complex and requires an unusually high level of medical expertise, coordinated multidisciplinary teams, and extensive supporting facilities. These are most effective when they are applied to a steady patient flow. For these reasons, the Cancer Control Program has encouraged the voluntary formation of groups of hospitals, each centered around an existing first-rate treatment program, to demonstrate modern treatment through consultation and education and to encourage the sharing of resources and where appropriate, referral of patients. These networks already treat more than ten percent of all childhood leukemias in the nation, and the number is expected to grow rapidly during the remainder of fiscal year 1974.

The Cancer Control Program, working with the American Cancer Society, has established 20 co-funded demonstration centers for the earlier detection of breast cancer. These demonstration centers are now examining women at a rate of 100,000 per year, but the real target is all women old enough to have a high risk of breast cancer. These 20 demonstration programs, with increases planned for early fiscal year 1975, should lead to a rapid increase in the proportion of breast cancers diagnosed while curative treatment is still possible.

The Cancer Control Program is also supporting projects to determine the potential effectiveness and impact of applying new methods for the early detection of lung cancer. If the methods appear to be feasible, they will result in the immediate development of a large-scale demonstration program.

The combined effects of cancer and its treatment sometimes leave serious physical defects, deformities, impaired or absent function, and a host of problems related to employment, return to previous personal activities, and psychological damage. There has not been enough attention paid to the long-term problems of returning cancer patients to their work and to society. The Cancer Control Program is supporting an aggressive program to change this situation, including improvements in physical therapy, occupational therapy, care of ostomies (artificial body openings for breathing, excretion, etc.), and the restoration of acceptable appearance and function after the physical damage caused by cancer of the head and neck. Most important, perhaps, was the funding of seven projects to provide for the demonstration of improved organization and availability of all these rehabilitation services, and others, through both community hospitals and major medical centers.

The Cancer Control Program is working with the National Clearinghouse for Smoking and Health to develop and support cancer-related projects in education, demonstration, and assistance to persons who want to stop smoking. The two agencies are jointly supporting the demonstration and evaluation of education on smoking in 90 school districts and communities by national organizations concerned with medicine, public health, and public education.

The effective control of cancer requires an informed public as well as an adequate number of well-qualified persons in a variety of cancer-related professions. The Cancer Control Program is supporting a variety of educational activities: an international conference on smoking; a telephone inquiry system for physicians, and a separate telephone system for the public; additional training of nurses in the care of cancer patients; and catalogs of books, films, and other teaching materials related to cancer for use by selected health professionals. A study of recent ongoing cancer public education programs is already providing useful information for the design of future programs.

NATIONAL INSTITUTES OF HEALTH

National Cancer Institute

Program Purpose and Accomplishments

Activity: Cause and prevention research (Public Health Service Act, Title IV, Part A)

1974		1975		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
638	$133,481,000	1/	647	$151,662,000

Purpose: Included within this activity is the national program for research contained in the first four objectives of the National Cancer Program Plan. These objectives are: (1) to reduce the effectiveness of cancer producing agents; (2) to modify body mechanisms so as to minimize the hazards of cancer inducing agents; (3) to prevent transformation of normal cells to cells capable of forming cancers; and (4) to prevent progression of precancerous cells to cancers, the development of cancers from precancerous conditions, and spread of cancers from primary sites.

Explanation: Research in this area is conducted in government laboratories and in academic and private institutions. Research in the academic and private sector is accomplished through the funding of both research grants and research and support contracts. Cause and prevention research includes viral, carcinogenic, and demographic research. Those selected activities that are performed within the breast, lung, large bowel, bladder and prostate task forces are also identified within this research area.

Accomplishments in 1974: In 1974, significant accomplishments included the following: (1) Epstein-Barr virus, which is associated with Burkitt's lymphoma and mononucleosis, was shown to cause cancer in primates. (2) Rapid and sensitive biochemical tests have been developed for detecting virus activity in cancerous cells. This is of particular importance for screening high risk human populations. (3) Initial definition of some characteristics of less hazardous cigarettes has been attained. (4) Research in the lung cancer program has provided methods which permit investigators to study morphologic changes and biochemical events directly on respiratory epithelium in animals and human tissues. (5) It was discovered that high beef consumption might possibly be related to higher rates of cancer of the large intestine in Japanese immigrants and Japanese descent Americans as opposed to rates in Japan. (6) An advanced systems laboratory, responsive to the needs of new research findings, for utilization by visiting scientists from all over the world, has been established at the Frederick Cancer Research Center.

Objectives for 1975: Research will be increased in the search for viruses as a cause of cancer in man. There will be further identification and investigation of high-risk populations to cancer. Increased efforts will be pursued to improve assessment of carcinogenic potential of environmental and industrial chemicals and further characteristics of less hazardous cigarettes will be defined. Additionally, the level of research on the immune responses to tumor viruses and to carcinogens will be expanded.

1/ Authorization expires June 30, 1974; extension legislation is proposed.

NATIONAL INSTITUTES OF HEALTH

National Cancer Institute

Program Purpose and Accomplishments

Activity: Detection and diagnosis research (Public Health Service Act, Title IV, Part A)

1974		1975		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
161	$37,249,000	1/	168	$41,744,000

Purpose: As described in Objective 5 of the National Cancer Program Plan, the goals of detection and diagnosis research are to develop the means to achieve an accurate assessment of (a) the risk of developing cancer in individuals and in population groups and (b) the presence, extent and probable course of existing cancers.

Explanation: Identified with the goals of this research are three general areas of investigation; detection, diagnosis and prognosis. In detection, studies are under way to identify population groups with high risk to cancer, conditions associated with cancer, as well as developing procedures for screening population groups for cancer. Diagnosis research deals with improving procedures to determine the presence and location of cancer in individuals. Prognosis encompasses the determination of cancer characteristics that cause different growth rates and probability of spread to predict the course of cancer in individuals. Research in this area is conducted in government laboratories and academic and private institutions. Research in the private community is accomplished through the funding of research grants and research and support contracts.

Accomplishments in 1974: In detection research, the use of cytologic screening for cervical cancer has been extended to other high risk groups. A major program is under way to develop machines capable of assisting the pathologist in reading the vastly increasing number of cytologic specimens. Prototype machines have been developed which separate normal cells from those suspicious of cancer. In diagnosis, using flexible fiberoptic endoscopes, small tumors invisible by x-ray can be found anywhere in the large bowel and in a large part of the bronchial tree, at a stage when surgery should cure them. Also, the first immunodiagnostic test for cancer has become available to the general medical profession, a radioimmunoassay method for carcinoembryonic antigen (CEA). Two additional radioimmunoassays have demonstrated usefulness in diagnosing testicular tumors. In prognosis research, a recent exciting finding under intensive study is the demonstration of the "tumor angiogenesis factor", a substance produced by experimental tumors that promotes the growth of blood vessels into them, permitting growth beyond just a tiny nodule.

Objectives for 1975: Scientists will continue to develop automated methods and machines for cancer cytology. Another promising area to be supported is the identification of tumor antigens for screening tests and in the development of tests for hormones produced in some tumors. Also, work will start on a specific test for human blood in the feces which would provide a simple method for screening for bowel cancer. An effective method will be sought for bowel cleansing before a barium enema to facilitate the diagnosis of bowel cancer.

1/ Authorization expires June 30, 1974; extension legislation is proposed.

NATIONAL INSTITUTES OF HEALTH

National Cancer Institute

Program Purpose and Accomplishments

Activity: Treatment research (Public Health Service Act, Title IV, Part A)

1974		1975		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
647	$178,674,000	1/	653	$203,128,000

Purpose: Included within this activity is the national program for research in treatment of patients with cancer. The primary goal of Objective 6 of the National Cancer Program Plan is to "develop the means to cure as many patients as possible and to maintain maximum control of the cancerous process in patients not cured." The National Cancer Institute serves as the focal point for research in cancer treatment in this country and probably the world.

Explanation: Research in this area is conducted in government laboratories and in academic and private institutions. Research in the academic and private sector is accomplished through the funding of both research grants and research and support contracts. Efforts are underway to expand existing and initiate additional clinical cooperative groups to investigate anti-cancer therapies. Research treatment by the use of surgery, radiation and chemotherapy either used singly or in combination is a major segment of present research efforts.

Accomplishments in 1974: In 1974, significant accomplishments included the following: (1) Use of combination treatment produced complete remissions in 45% of patients treated for advanced non-Hodgkin's lymphoma. (2) Surgery followed by radiotherapy has increased the rate of five-year survival in women with advanced cancer of the lining of the uterus. (3) Drug treatment combined with radiotherapy has produced temporary objective tumor shrinkage and improvement in patients with small cell carcinoma of the lung, usually the most aggressive lung tumor. (4) Fifteen new materials have been approved for study against human cancer.

Objectives for 1975: Efforts will be intensified to apply all available knowledge and experience to the management of patients with the slowly growing tumors that account for 70-80% of all cancer deaths. There will be extensive use of surgery and/or radiotherapy with chemotherapy and/or immunotherapy since combinations of modalities have proven superior to agents used alone in disseminated disease. Phase II (therapeutic effectiveness) studies that include brain tumors, lung, breast, colon, ovarian, and testicular cancers will be broadened to include cancer of the cervix, prostate, pancreas, and bladder. Phase III studies comparing various remedies are under way in breast cancer, lung cancer, lymphomas, testicular tumors, ovarian cancer and colon cancer. In 1975, these studies will be expanded to include head and neck, bladder and prostate cancer.

1/ Authorization expires June 30, 1974; extension legislation is proposed.

NATIONAL INSTITUTES OF HEALTH

National Cancer Institute

Program Purpose and Accomplishments

Activity: Cancer biology (Public Health Service Act, Title IV, Part A)

1974			1975	
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
317	$77,488,000	1/	321	$89,321,000

Purpose: Cancer Biology is an area of research which provides fundamental information on the cause and nature of cancer in man, with the expectation that this will result in better methods of prevention, detection and diagnosis, and treatment of neoplastic diseases.

Explanation: This program consists of basic research in all fields of cancer supported through research in government agencies as well as through grant and contract awards. It includes research that cannot reasonably be classified in any of the specific research thrusts but where results have potential application to all thrusts.

Accomplishments in 1974: Considerable progress has been made in enhancing various components of the immune system in cancer patients. During the past year, several chemicals have been isolated which can be used to alter cell behavior in tissue culture. By changing the chemical environment in which the cells are grown, normal cells were made to assume the growth pattern of cancer cells, and cancer cells have been made to behave normally. Progress in determining the portion of the nuclear DNA responsible for continuous gene repression has been encouraging. The molecular working of the cell can now be probed to analyze the events leading to the failure of growth repression which characterizes cancer cells.

Objectives for 1975: The increase of funding in 1975 will permit the initiation of important new studies in cell hybridization, cell suppression and reversal of malignant cell growth. Other work to be done includes new procedures to isolate pure cultures of mammalian cells, including tumor cells. Humoral and cell bound antibodies will be studied extensively in order to understand the basic phenomena involved in diagnosis, prevention and treatment of neoplasia. Also, efforts will be focused on the characteristic biochemistry of the cancer cell and the influence of cancer on the biochemistry of the host.

NATIONAL INSTITUTES OF HEALTH

National Cancer Institute

Program Purpose and Accomplishments

Activity: Cancer centers support (Public Health Service Act, Title IV, Part A)

1974			1975	
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
12	$19,578,000	1/	14	$23,484,000

Purpose: The cancer centers support activity includes exploratory projects and core grants only. Exploratory projects are designed to determine the feasibility of establishing specialized and comprehensive cancer centers. Core grants are used to assist in the support of the administration, common services and collaborative activities of cancer centers.

Explanation: Comprehensive Cancer Centers are established to conduct long term multidisciplinary programs related to cancer. The dollars for research performed at cancer centers are reflected under the appropriate research areas of cause and prevention, detection and diagnosis, treatment and cancer biology. The core grant assists in the support of the operating and administrative expenses of these centers. Exploratory projects, awarded through the grant mechanism, also assist in the planning and development aspects prior to the establishment of a cancer center.

Accomplishments in 1974: Currently, the NCI has recognized 12 Comprehensive Cancer Centers. By the end of 1974, it is expected that six additional centers will be recognized, to a total of 18. This includes three Comprehensive Centers that were identified before the National Cancer Act of 1971 was passed. Planning is now under way in many areas throughout the country to determine the feasibility of the establishment of cancer centers.

Objectives for 1975: Feasibility studies for cancer centers will continue to be encouraged. Continued emphasis will be placed on core support for cancer centers commensurate with the expansion and development of the cancer centers program.

1/ Authorization expires on June 30, 1974; extension legislation is proposed.

NATIONAL INSTITUTES OF HEALTH

National Cancer Institute

Program Purpose and Accomplishments

Activity: Research manpower development (Public Health Service Act, Title IV, Part A)

1974			1975	
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
8	$18,530,000	1/	8	$22,530,000

Purpose: The Research Manpower Development program provides support for fellowships and training grants in various scientific fields related to cancer research, as well as the new Clinical Education Program which is designed to create more innovative education programs in medical schools.

Explanation: Through the use of the grant mechanism, awards are made to individuals (in the form of fellowships) and to institutions in support of training and education programs in the sciences related to cancer research.

Accomplishments in 1974: During 1974, the Institute awarded 432 fellowships and 169 graduate and clinical training grants. These awards included such disciplines as radiation, immunology and cancer biology.

Objectives for 1975: It is estimated that approximately 930 individuals will be supported through fellowship awards. In addition, the Clinical Education Program will provide resources for the award of 67 grants including awards to schools of medicine, dentistry, and osteopathy.

1/ Authorization expires June 30, 1974; extension legislation is proposed.

NATIONAL INSTITUTES OF HEALTH

National Cancer Institute

Program Purpose and Accomplishments

Activity: Construction (Public Health Service Act, Title IV, Part A)

1974			1975	
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
11	$30,790,000	1/	11	$22,317,000

Purpose: Within the provisions of the National Cancer Act of 1971, construction authority was provided to the National Cancer Institute. The intent of the program is to create additional facilities as well as to improve existing facilities essential to the expanding cancer program.

Explanation: Construction awards will be made utilizing primarily the grant mechanism. The National Cancer Institute intends to pay up to 75% of the cost of construction for cancer research centers.

Accomplishments in 1974: In 1974, $30,790,000 supported the upgrading and construction of approximately eight facilities, four being comprehensive centers. Also, $4,275,000 has been specifically earmarked for the Norris Cotton Cancer Research Center. In addition to the construction grants for centers, contract activities include improvement of the Frederick Cancer Research Center and modernization and upgrading of facilities on the NIH campus.

Objectives for 1975: Funds totalling $22,317,000 are requested for modernization and renovation of cancer research centers, biohazard facilities, facilities on the NIH campus and at other research facilities, including the Frederick Cancer Research Center.

1/ Authorization expires June 30, 1974; extension legislation is proposed.

NATIONAL INSTITUTES OF HEALTH

National Cancer Institute

Program Purpose and Accomplishments

Activity: Cancer control (Public Health Service Act, Title IV, Part A)

1974		1975		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
44	$34,599,000	1/	51	$45,814,000

Purpose: The Cancer Control Program of the National Cancer Institute came into being with the signing of the National Cancer Act of 1971. Its general purpose is to bridge the gap between research and application in the practice of medicine and public health so as to minimize illness and death from cancer.

Explanation: The major objectives of the program are to take cancer research outputs in prevention, diagnosis, treatment and rehabilitation, and demonstrate their effectiveness in controlled community groups; communicate the successful R&D and demonstration findings to the practitioners of medicine and public health; educate practitioners and laymen about the latest cancer research findings; and stimulate the general application of effective control measures.

Accomplishments in 1974: In 1974, the Cancer Control Program funded major program activities in the fields of prevention, screening, diagnosis, treatment, rehabilitation, and education. A network of hospitals was established to improve the treatment of childhood leukemia and of Hodgkin's Disease and lymphomas at all ages. The Cancer Control Program, working with the American Cancer Society, has established 20 demonstration centers for the early detection of breast cancer. The program is also supporting projects to determine the effectiveness and impact of new methods for the early detection of lung cancer. Cancer Control has initiated projects for the rehabilitation of cancer patients including improvements in physical therapy, occupational therapy and restoration of acceptable appearance and functions after the physical damage caused by cancer. Through this grant mechanism a program has been established to support local initiatives in community outreach.

Objectives for 1975: In addition to the expansion of work initiated in 1974, the Cancer Control Program will deal with the following areas: (1) projects in the control of cancer-related occupational hazards; (2) projects directed toward the reduction of lung cancer; (3) additional projects to improve the early detection of breast and cervical cancers; (4) high-priority projects concerned with delivering optimal cancer treatment for several additional forms of cancer; and (5) additional projects in rehabilitation.

1/ Authorization expires June 30, 1974; extension legislation is proposed.

New Positions Requested

	1975 Grade	1975 Number	1975 Annual Salary
Research			
Medical Officer	GS-15	1	$28,263
Health Scientist Administrator	GS-14	2	48,494
Health Scientist Administrator	GS-13	3	62,031
Scientist	GS-13	2	41,354
Health Scientist Administrator	GS-13	1	20,677
Scientist	GS-12	2	34,994
Biologist	GS-11	1	14,671
Grants Management Specialist	GS-11	1	14,671
Administrative Assistant	GS-9	1	12,167
Grants Management Specialist	GS-7	1	9,969
Medical Technician	GS-7	3	23,307
Secretary	GS-5	5	40,275
Clerk-Typist	GS-4	2	14,396
Clerk-Typist	GS-3	1	6,408
		26	371,677
Resource Development			
Health Scientist Administrator	GS-15	1	28,263
Secretary	GS-5	1	8,055
		2	36,318
Cancer Control			
Scientist	GS-14	1	24,247
Staff Assistant	GS-12	2	34,994
Contract Specialist	GS-12	1	17,497
Secretary	GS-5	1	8,055
Clerk-Typist	GS-4	2	14,396
		7	99,189
Total new positions, all activities		35	507,184

Tuesday, March 26, 1974.

NATIONAL HEART AND LUNG INSTITUTE

WITNESSES

DR. THEODORE COOPER, DIRECTOR

DR. ROBERT S. STONE, DIRECTOR, NATIONAL INSTITUTES OF HEALTH

DR. DeWITT STETTEN, JR., DEPUTY DIRECTOR FOR SCIENCE, NATIONAL INSTITUTES OF HEALTH

DR. ROBERT L. RINGLER, DEPUTY DIRECTOR, NATIONAL HEART AND LUNG INSTITUTE

LYMAN MOORE, EXECUTIVE OFFICER, NATIONAL HEART AND LUNG INSTITUTE

JOHN H. REEDER, FINANCIAL MANAGEMENT OFFICER, NATIONAL HEART AND LUNG INSTITUTE

LEON M. SCHWARTZ, ASSOCIATE DIRECTOR FOR ADMINISTRATION, NATIONAL INSTITUTES OF HEALTH

LELAND B. MAY, ACTING DIRECTOR OF FINANCIAL MANAGEMENT, NATIONAL INSTITUTES OF HEALTH

CHARLES MILLER, DEPUTY ASSISTANT SECRETARY, BUDGET

Object Classification (in thousands of dollars)

	Identification code 09-25-0872-0-1-651	1973 actual	1974 est.	1975 est.
	Direct obligations:			
	Personnel compensation:			
11.1	Permanent positions	9,863	10,567	11,348
11.3	Positions other than permanent	668	702	733
11.5	Other personnel compensation	301	320	331
	Total personnel compensation	10,832	11,589	12,412
12.1	Personnel benefits: Civilian	1,445	1,539	1,621
21.0	Travel and transportation of persons	729	784	828
22.0	Transportation of things	110	160	204
23.0	Rent, communications, and utilities	735	825	1,161
24.0	Printing and reproduction	249	300	345
25.0	Other services	71,972	124,107	97,751
26.0	Supplies and materials	2,875	3,141	3,180
31.0	Equipment	1,272	1,459	1,459
41.0	Grants, subsidies, and contributions	165,503	185,597	190,338
	Total direct obligations	255,722	329,501	309,299
	Reimbursable obligations:			
21.0	Travel and transportation of persons	6	10	10
99.0	Total obligations	255,728	329,511	309,309

Personnel Summary

	1973 actual	1974 est.	1975 est.
Total number of permanent positions	649	665	663
Full-time equivalent of other positions	51	51	51
Average paid employment	700	696	738
Average GS grade	8.5	8.6	8.6
Average GS salary	$14,260	$15,138	$15,473
Average salary of ungraded positions	$11,138	$12,018	$12,253

Program and Financing (in thousands of dollars)

Identification code 09-25-0872-0-1-651	1973 actual	1974 est.	1975 est.
Program by activities:			
Direct program:			
1. Heart and vascular diseases	146,910	197,048	174,217
2. Lung diseases	28,915	44,567	45,340
3. Blood diseases and resources	42,098	50,952	50,309
4. Intramural laboratory and clinical research	19,267	21,651	22,445
5. Research management and program services	12,110	15,283	16,988
Total direct program	249,300	329,501	309,299

Program and Financing (in thousands of dollars)

	Identification code 09-25-0872-0-1-651	1973 actual	1974 est.	1975 est.
	Reimbursable program:			
	4. Intramural laboratory and clinical research	6	10	10
	Total program costs, funded [1]	249,306	329,511	309,309
	Change in selected resources (undelivered orders)	6,422	---------	---------
10	Total obligations	255,728	329,511	309,309
	Financing:			
11	Receipts and reimbursements from: Non-Federal sources	−6	−10	−10
25	Unobligated balance lapsing	44,320	---------	---------
	Unobligated balance restored	---------	−43,036	---------
	Budget authority	**300,042**	**286,465**	**309,299**
	Budget authority:			
40	Appropriation	300,000	302,915	309,299
	Withheld from obligation and expenditure (Public Law 93-192)	---------	−13,365	---------
41	Transferred to other accounts	---------	−3,085	---------
42	Transferred from other accounts	42	---------	---------
43	**Appropriation (adjusted)**	**300,042**	**286,465**	**309,299**
	Relation of obligations to outlays:			
71	Obligations incurred, net	255,722	329,501	309,299
72	Obligated balance, start of year	175,520	197,768	221,468
74	Obligated balance, end of year	−197,768	−221,468	−196,988
77	Adjustments in expired accounts	−553	---------	---------
90	Outlays	232,921	305,801	333,779

[1] Includes capital outlay as follows: 1973, $1,145 thousand; 1974, $1,170 thousand; 1975, $1,260 thousand.

NOTES

Excludes $5,618 thousand in 1974 and $4,618 thousand in 1975 for activities transferred to (in thousands of dollars):

	1974	*1975*
Research Resources	2,435	2,435
Office of the Director	98	98
Departmental management	85	85
Health Resources	3,000	2,000

Comparable amounts for 1973 ($11,332 thousand) are included above.

Excludes $77 thousand in 1975 for activities transferred to Office of the Assistant Secretary (Health). Comparable amounts for 1973 ($77 thousand) and 1974 ($77 thousand) are included above.

Includes $423 thousand in 1975 for activities previously financed from (in thousands of dollars):

	1973	*1974*
National Institute of General Medical Sciences	358	358
Departmental Management	3	3

Mr. Flood. Now we have the National Heart and Lung Institute of the National Institutes of Health. The presentation will be made by Dr. Theodore Cooper, the Director.

We have your biographical sketch which we will place in the record.

[The biographical sketch follows:]

Department of Health, Education, and Welfare

NATIONAL INSTITUTES OF HEALTH, NATIONAL HEART AND LUNG INSTITUTE

Name.—Theodore Cooper, M.D.

Position.—Director, National Heart and Lung Institute.

Birthplace and date.—Trenton, N.J., December 28, 1928.

Education.—June 1946, graduated from high school; June 1949, B.S., Georgetown University; June 1954, M.D., St. Louis University; 1956, Ph. D., St. Louis University.

Experience.—1968 to present: Director, National Heart and Lung Institute.

1967–68.—Associate Director for artificial heart-myocardial infarction program—National Heart Institute.

1966–68.—Professor and chairman, Department of Pharmacology and Professor of Surgery, University of New Mexico School of Medicine.

1964–66.—Professor of surgery, St. Louis University.

1962–64.—Associate professor of surgery, St. Louis University.

1961–65.—Director, Center for Cardiovascular Research, St. Louis University.

1960–62.—Assistant professor of surgery, director section of surgical physiology, St. Louis University.

1959–60.—Surgeon, U.S. Public Health Service, National Heart Institute.

1958–59.—Assistant resident in surgery, St. Mary's Group of Hospitals, St. Louis University.

1956–58.—S.A. surgeon, U.S. Public Health Service, National Heart Institute.

1954–55.—Intern, St. Mary's Group of Hospitals, St. Louis University.

Association memberships.—American Society for Clinical Investigation, American Physiological Society, Society for Experimental Biology and Medicine, American Society for Pharmacology and Experimental Therapeutics, Society of Sigma XI, International Cardiovascular Society, American College of Chest Physicians, American Society of Artificial Organs, American Federation for Clinical Research, American Association of University Professors, American Association for Advancement of Science, American College of Cardiology.

Special awards citations, or publications.—Borden Award—St. Louis University, 1954; Who's Who in American Colleges and Universites, 1956; Research Development Award, USPHS, 1962–66; author or coauthor of approxmately 150 publications. Editorial board, circulation, American Journal of Physiology, Journal of Applied Physiology, editorial board, Journal of Pharmacology and Experimental Therapeutics, Circulation Research, Journal of Molecular Cardiology. DHEW Superior Service Honor Award, 1972. St. Louis University Alumni Merdit Award, 1972, 16th honorary Lecture Award, Albany Medical College, Albany, 1972. Gold Heart Award, American Heart Association, 1973.

Mr. Flood. Is there anybody here you want us to meet now?

Dr. Cooper. Yes, sir. I have with me Dr. Robert Ringler, Deputy Director of the Institute: Mr. Lyman Moore, Executive Officer of the Institute; and Mr. John Reeder, the Financial Management Officer of the Institute.

Mr. Flood. I see you have a statement. How do you wish to proceed?

Dr. Cooper. If it is appropriate, sir, I would like to read my statement first.

Mr. Flood. Suppose you do.

OPENING STATEMENT

Dr. Cooper. Mr. Chairman, and members of the committee: I am pleased to have this opportunity to meet with you. The Institute is submitting a detailed report of current activities and accomplishments and an updated 5-year plan as required by Public Law 92–423. My comments today constitute a brief summary of this document. The National Heart and Lung Advisory Council has also prepared its annual report.

One of the news analysts recently said, only the bad news seems to make news. In reporting to you, I think we may have been guilty of this in the past. We have emphasized the fact that more than 27 million people in this country have heart disease; that 1.2 million die of these diseases each year, 700,000 of them from heart attacks alone: and 25 percent of these deaths are people under the age of 65. We have brought to your attention the fact that over 23 million people of all ages have high blood pressure—hypertension. Only 50 percent of them know that they have high blood pressure and only one-quarter of these, perhaps 3 million, are getting adequate therapy. We have identified many areas where we lack knowledge, knowledge that can only come from continuing and intensified research. You know that we need more trained people to do this research and to take the results of the research to the people in the form of better medical care and more effective prevention.

All this is still true. But this is the negative side of things, the bad news. I'd like to bring you some good news today. Of course, I wish I had even more good news than I do. But I am not going to overpromise nor magnify our achievements. I don't have to. The facts speak for themselves.

The first of these is that, despite the above statistics, for the first time in a quarter of a century, deaths from coronary heart disease have leveled off and appear to be descreasing. The initial decreases are not dramatic, but they are hopeful.

The stemming of what has been called the 20th century epidemic is the result of many things: better diagnosis, new drugs, pacemakers, surgery, transfusion technology, antibiotics, and an understanding of risk factors. These have made initial approaches to prevention possible. Current research results indicate that we should soon have more and better methods of treatment and prevention. Specifically, new practical methods have been devised to locate and measure the area or amount of injury to the heart muscle that follows a heart attack. Ability to measure the amount of damage has spurred activities to limit the extent of the damage which follows upon blockage of a coronary artery. Tests are now being run in experimental animals to evaluate these methods, some of which are chemical, some pharmaceutical, and some mechanical. A number of the techniques are beginning to be evaluated in patients.

A new, noninvasive technique used, ultrasonics, called echocardiography, also promises to increase the capability of physicians to make more precise, yet less expensive, important diagnoses.

CORONARY DRUG PROJECT

The coronary drug project, which has been studying the effectiveness of five different drugs in the prevention of a second heart attack in more than 8,000 men, has already shown that three of the drugs under test do not help the patient by either preventing a second heart attack nor lessening the seriousness of the second episode. Therefore, these drugs have been eliminated from the trials. During this fiscal year, all the necessary data on the remaining two drugs will have been collected and some of the final analyses performed. To eliminate three drugs may not strike you as a piece of good news. But let me assure you that it is very important news, for had this trial not been conducted then, hundreds, indeed thousands, of patients would have been treated in good faith by conscientious physicians with drugs which appear to be of no real benefit.

LIPID RESEARCH CLINICS

Twelve Lipid Research Clinics have been established to determine what proportion of the population have an abnormality of their blood fats, known as type II hyperlipidemia and who are thereby, at a markedly increased risk of a heart attack during the early adult years. The LRC's are also beginning to recruit some 4,000 patients who have this disorder of their blood fats but who have not yet had a heart attack. In a carefully controlled closely knit study we will determine whether or not lowering serum lipids (blood fats) reduces the risk of heart disease and if so how much the lipids need to be lowered and what is the best way to accomplish this.

A separate network of some 20 clinics has been established to study 12,500 patients who have several risk factors in order to see how much effect we can have on their risk of a heart attack if simultaneously the patient stops smoking, lowers his serum cholesterol or blood lipids, and reduces his blood pressure. All of these clinical trials are most important since each addresses a distinct group of people known to be at high risk of heart disease and, in view of the magnitude and urgency of the problem of heart disease in this country, we must know as soon as possible what the best therapy or prevention is for these people who have different combinations of risk factors. These studies will also tell us whether or not we can afford the luxury of waiting until adulthood or middle age to attempt to reduce risk factors of whether these must be prevented from the very beginning.

Because a heart attack or a stroke can, and does, occur in people who are only 20 or 30 years of age, we have underway a number of new studies to determine how prevalent the risk factors are in children and teenagers and how soon can be certain whether or not a child born to parents with abnormal lipids will also suffer from this disorder. If therapy must be begun in childhood and this therapy involves drugs, then there are a large number of problems surrounding long-term drug administration to the growing child that must be resolved.

I would like to underscore the success that some of our investigators in our specialized centers of research have had in developing a simple, rapid, and economical method for measuring serum lipids. This is a semiautomated technique. The equipment costs approximately $5,000 The cost of the test supplies is 1 cent. When a new technique such as heart transplants is introduced much is written about the cost of the new procedure. I am not aware that anything has been written for the ordinary public about this new test which is both reliable and inexpensive.

Similarly, we do not only test new or esoteric drugs. Currently underway is a test of the effectiveness of aspirin in preventing blood cells from sticking together to form thrombi or clots. When these appear in the coronary vessel the patient experiences a heart attack; when they appear in the vessels to the lung he has a pulmonary embolus and I might add when they appear in the blood vessels to the head he experiences perhaps a stroke or an ischemic attack. All of these conditions can be and often are lethal.

Studies of hormones like angiotensin, prostaglandins in the blood show promise of revealing how high blood pressure develops and thus how it may be controlled through the development and use of appropriate new and specific drugs.

HIGH BLOOD PRESSURE EDUCATION PROGRAM

We have had excellent success in bringing awareness to the public and new data to the health professions in our new national high blood pressure education program in which we have involvement with all segments of society. Studies of the walls of arteries and veins, studies of the different kinds of cells in these walls, of their biophysical and molecular structure as well as the function of the cells, may reveal how fat in the blood actually contributes to disease in the blood vessel wall. Synthetic materials like polyurethane and styrene and new ways of handling previous materials, by making better bonds, introducing blocks, prolonging flex life or producing a better living surface are some of the reasons why a better temporary or partial artificial heart substitute can now be developed.

CHRONIC LUNG DISEASE

Our program is not limited to cardiovascular disease. Public Law 92–423 emphasized the need for us to expand our efforts in chronic lung disease, in certain of the blood diseases, notably sickle cell disease, and in blood banking.

Since 1970, our support for research in chronic lung disease has increased fivefold. In my view, we are entering a new era of research on the lung. No longer are the activities limited to the study of the process of ventilation and gas exchange. Modern molecular, cellular, immunological, and biochemical techniques are being increasingly utilized. Our approach to the prevention and treatment of respiratory distress syndromes, bronchitis, emphysema, and pulmonary vascular disease will be revolutionized. Again my optimism is based on current research. For example:

We are learning which cells of the lung make collagen, an important substance both in normal tissue and in several disease states.

Much of the technology and "know-how" developed in the artificial heart program has been useful in developing and improving respirators or artificial lungs for patients who range all the way from premature babies through acutely ill young adults to older folks suffering from respiratory failure or insufficiency.

We already know that as many as 90 percent of infants who suffer respiratory distress or hyaline membrane disease, after a birth which is often premature, can be successfully tided over the days of inadequate function or immaturity of their own lungs, to the point where the babies' lungs can take over and the baby breathe normally. Furthermore, we now know that these babies, when they become older infants and young children show every evidence of a complete cure of their lung disease and no signs of any undesirable side effects. This is in marked contrast to the outlook for these youngsters, who as recently as 5 years ago when a large number, much more than half, of them died as newborns and many of those who survived had permanent brain damage and mental retardation.

Individuals who lack certain enzymes in their blood and thus are prone to a particular lung disorder can now be identified through blood testing long before they have suffered any damage to their lungs. The significance of this becomes apparent when you realize that we have no cure, as yet, for such diseases as emphysema or pneumoconiosis or black lung disease. In an attempt to prevent this disorder, we are supporting promising work that deals with the reaction of lung cells to foreign particles such as coal dust, or silica dust, or asbestos. Once we know what the cell does, how it reacts to these foreign particles, air pollutants, then we are almost certain to have available a line of attack to prevent the onset, or the further development, of this disease.

SICKLE CELL DISEASE

Earlier I mentioned the study of drugs in coronary heart disease and our findings that three of them were ineffective. In the sickle cell disease program we have now determined that treatment of a sickle cell crisis—an episode of acute, intense pain often followed by deformity of arms or legs—treatment of this crisis by a substance knows as urea does not appear to be effective in relieving the crises nor preventing the sequelae. We have hope that other chemicals that react with the abnormal hemoglobin may prove to be useful in treating this disease or this manifestation. But again, it is as important to know what will *not* work as to establish what *will.*

Despite all the refinements in public information and communication techniques developed in recent years, we have found that there is a great deal to be learned about how best to approach the public and the profession to alert them to the possibility of chronic and indeed often silent disease, to encourage them to adopt preventive measures while, at the same time, insuring that they are not handicapped socially, vocationally, nor economically, by the knowledge that they are at risk of disease themselves or may pass on a disease to their children.

This is not only true in the area of sickle cell disease, I might say parenthetically, but also in high blood pressure and in many of the heart diseases as well.

BLOOD BANKING POLICY

The Blood Diseases and Resources Division of the National Heart and Lung Institute has been working closely with other members of the Department and with other sectors of society including voluntary agencies, professional associations, organized labor and pharmaceutical industries to develop a new national blood banking policy. The goal of this policy is to find more efficient and safer ways to utilize precious blood resources.

This policy is in process of implementation at the present time.

One of the ways of increasing the efficient use of this human tissue is through better fractionation or division of the blood, storage, and administration of the many different "factors" that are to be found in whole blood. Factor VIII for instance, is a factor lacking in patients with hemophilia, a disease characterized by a tendency to bleed after the slightest injury into joints or organs of the body. Up to now the cost of extracting and administering this factor from donated whole blood has been so high that hemophilia in the family was an economic disaster. Current research has revealed a new way to extract this factor and we are pleased to report this year we are encouraged that the results indicate that we should be able to double the yield of it and we hope that this will result in effectively cutting the cost in half.

Obviously in these few minutes I have only presented examples of the Institute's program. Over the past 25 years the application of the results of research in heart disease has saved some 3 million lives. I think you can see that our activities are cost effective not solely in lives saved and suffering prevented but in reducing the costs of therapy and rehabilitation. I have tried to select examples which also show how patient needs and disease problems trigger research investigations; while research findings in turn affect treatment and provide the basis for prevention.

HEALTH INFORMATION

There are two other essential components of the Institute's program that I have not mentioned. The first of these is in the area of health information both for professionals and for the public. An Assistant Director for health information has been recruited as directed by section 413 of Public Law 92–423. He is working to develop information resources within the Institute and to dovetail these with informational endeavors of other agencies and non-Federal segments of our society such as voluntary agencies, organized labor, and industrial corporations, et cetera.

I did note in passing that there were three areas in which we were already successfully working on this application, high blood pressure, sickle cell disease, and blood banking. There are others.

These efforts have been enthusiastically received by the scientific, medical, and lay communities. I have already cited some of the examples. I would add only work on food composition, on diet therapy, on pneumoconiosis, and cough.

Health information will be an important component of the new Research and Demonstration Centers. The Centers were authorized in section 415 of Public Law 92–423. They will not only make interdisciplinary research in heart, lung, and blood diseases more effective, we hope, in the Centers where they are located, but we hope they will serve as a national resource for trying out new methods of education, new techniques of therapy, and better ways to reach and to motivate those people who are at risk of disease.

In compliance with Public Law 92–423, 15 percent of our resources for research are being directed to lung problems and over 15 percent to blood disease problems. This has resulted in a change of emphasis within the Institute's program. It will be important to monitor the impact of this formula requirement on the overall program.

ALLOCATION OF RESOURCES

Last year you were concerned about the balance of our programs with respect to the use of grants and contracts as instruments of support. During the current year regular research and training fellowships and grants received 40 percent of the funds in our extramural research program. These grants underwrite the work of individual investigators. Program projects and specialized centers of research received 30 percent. These grants support groups of investigators who also themselves have proposed interdisciplinary studies of their own germination. All contracts, which pay for development, for fixed protocol clinical trails, and for some special time limited research studies, which the Institute feels are necessary, received 30 percent of our extramural dollars.

In conclusion, Mr. Chairman and members of the committee, the NHLI is asking for $309 million for fiscal year 1975 to continue the national heart, blood vessel, lung and blood program. This request represents an increase of $23 million over our fiscal year 1974 budget authority. I will be pleased to give you additional information, or to answer any questions you or the committee might have.

CORONARY DISEASE

Mr. Flood. You say in this statement that for the first time in 25 years deaths from coronary disease have leveled off. Of course that is certainly very good news. But to what do you attribute the leveling off?

Dr. Cooper. I think several things have happened in the last 7 to 10 years. We have had better diagnosis. We have earlier diagnosis. We have had many methods of treatment like coronary open heart surgery, the use of antibiotics to treat and prevent rheumatic heart disease. We have had more effective treatment of the heart attack by the use of the coronary care unit. We have had more effective utilization of drugs which can treat high blood pressure, which is one of the important factors in anticipating heart failure, stroke, or indeed heart attack, and in the aggregate the identification of these factors, along with our understanding of things which may cause heart disease, have allowed us to get started with the prevention on a long-term basis and therefore I think we are beginning to see progress in the statistics.

MOBILE CORONARY CARE UNITS

Mr. Flood. Are you part of this development program in reaching out into the community ambulance services, training the local police force, the local ambulance service, for immediate attack when such a problem arises, if and when?

Dr. Cooper. We did not support any of the mobile coronary care units. These were supported by the regional medical program. However, we did work with them in providing a technical base of information that would be appropriate for training in that situation and appropriate therapy for it.

Mr. Flood. Is the United States still the second ranking nation in deaths from heart disease?

Dr. Cooper. To our best knowledge we rank second behind Finland, yes, sir.

FIVE-YEAR PLAN

Mr. Flood. The National Heart, Blood Vessel, Lung, and Blood Act of 1972 called for development of a plan. Last year, you remember, we asked you about this and you told us the plan would be submitted to Congress by May 20, 1973. Obviously you were a little bit optimistic about that because the plan was actually submitted on July 24, 1973.

Isn't that about right?

Dr. COOPER. About right, yes, sir.

Mr. FLOOD. What happened?

Dr. COOPER. It was delayed in transit.

Mr. FLOOD. Something funny happened on the way to the forum or something like that?

Dr. COOPER. I cannot detail what the steps of delay were but it was submitted on time and——

Mr. FLOOD. Submitted to whom?

Dr. COOPER. The process is that we submitted this to NIH. It is then reviewed at NIH. It is reviewed then at the Department and submitted to the President for transmittal to the Congress. The process I think is what took the time.

Mr. FLOOD. You are being very kind.

The plan calls for the expenditure of $311 million in 1974 and $365 million in 1975; right?

Dr. COOPER. That is correct?

Mr. FLOOD. Your budget request in 1975 is $309,299,000. That is considerably less than the plan recommended for 1975, of course, but it is approximately the amount which the plan recommends for 1974.

Well, that being so, wouldn't it be fair to say you are about a year behind schedule?

Dr. COOPER. On a professional judgment basis, I would say, yes, sir. I think that the plan represents a professional judgment that reflects what might be if all the national resource allocation permitted it—a rate at which the progress might take place.

As you point out, we would be perhaps 1 year behind that.

Mr. FLOOD. Wouldn't you say that the allocation of funds within your total budget for 1975 is pretty generally consistent with the plan?

Dr. COOPER. On a prorated basis?

Mr. FLOOD. Yes.

Dr. COOPER. I think our priorities fit the priorities expressed in the plan; yes, sir.

LUNG AND BLOOD DISEASES

Mr. FLOOD. The act requires that of the sums that are appropriated, not less than 15 percent must be spent on disease of the lung and not less than 15 percent be spent on disease of the blood.

What percentage of your budget is allocated to each of those two areas?

Dr. COOPER. In fiscal year 1974, 15 percent will be allocated to the lung, by the end of June 30, 1974, and approximately 17 percent in the blood.

Mr. FLOOD. You said 1974?

Dr. COOPER. 1974. Now, in 1975, our allocation will be approximately the same, percentagewise.

EARMARKING OF FUNDS

Mr. FLOOD. Let me ask you this: Does this kind of earmarking make any kind of sense from a scientific point of view?

Dr. Cooper. I think an unlimited formula of allocation of this type might be a real handicap. At the early stages of formulation of this program it could be a real advantage. In other words, I think in these initial years of developing particularly the lung program, the requirement to do this has been a real stimulus for us to do excellent development of the preliminary program, but I think we would have to gage any number, being 15 percent of any number, as a prudent judgment at that point in time. That is why, in my statement, I indicated that I think we will have to monitor the impact of that formula as the budget level changes over the subsequent years.

Mr. Flood. What, in your view, are likely to be the most productive ways to invest additional funds in heart, blood vessel, lung, blood diseases? In other words, what basic research, clinical trials, training, control programs, and so on?

Dr. Cooper. I would rather not give an either/or answer there, Mr. Chairman. I think what we would see as a good program to accomplish this would include a large commitment to basic research—the development of the necessary manpower to implement an expanded program as mandated.

We would also feel that, in the words that you use, it includes more than just research and we have to be more effective in applying some of the information that is developed in research. So I think the implementation of the control program in that sense will also be a more effective way of controlling, as you asked, the problems of heart disease, lung diseases, and the blood diseases for which we are responsible.

COOPERATIVE DRUG STUDY

Mr. Flood. You mentioned that the Cooperative Drug Study will be completed in 1975. Well, not right in that chair because we were in a different room, but you did tell us last year it would be completed in 1974.

What happened to that one? Something always seems to be happening to you fellows.

Dr. Cooper. No, sir. The actual followthrough of the 5 years of the 8,340 patients on the drugs will be completed during this period of time as I indicated. The analysis of the effects—these come in at different periods of time.

In other words, they all don't start at day one. By the end of this fiscal year, we will have studied all of the patients 5 years. We have already made a determination and stopped three drug regimens. We feel that in the winddown phase—in the final analysis phase, which will take 1975—the patients will not be in the study.

The cost of the study will be reduced. The final conclusions on the other two drugs and the final summary conclusions will be completed in that period of time. But the actual execution of the study will be completed this year.

Mr. Flood. Has this study been a worthwhile investment in your opinion?

Dr. Cooper. Yes, sir; I think it has been very valuable. In fact, it has set a model for the world on how to conduct a large-scale clinical trial of many thousands of patients. Tens of thousands had to be screened to achieve it. It has been a very effective study.

Mr. Flood. For the record, we want a statement describing the Cooperative Drug Study and then you put in its objectives, how many people have participated, the findings to date, and of course how much has been spent on it each year since it started, and what will be the ultimate total cost, for the record.

Dr. Cooper. Yes, sir.

[The information follows:]

Cooperative Study of Drugs and Coronary Heart Disease

(CORONARY DRUG PROJECT)

Background

Development of a study of the effect of lipid-lowering drugs on atherosclerotic heart disease was recommended by the National Advisory Heart Council in 1960. Planning funds were provided in 1961. Two years later, in the fall of 1963, applications from a coordinating center and from four clinical groups were submitted to implement a standardized protocol for this clinical trial. A year after their approval in 1964, line item funds were appropriated for the support of this project. Following the release of these funds in the spring of 1965, these first five grants were activated with assurance of support for 7 years. Patient recruitment began in March 1966. During the following 2 years 51 additional clinics were enrolled stepwise, and were also approved for 7 years each.

Objectives

The coronary drug project was undertaken to evaluate the efficiency of several lipid-lowering drugs in the long term treatment of coronary heart disease in men of ages 30 to 64 with (clearly defined) evidence of previous myocardial infarction, with respect to mortality, cardiovascular morbidity, changes in serum lipids and other biochemical factors, electrocardiographic changes, and side effects. The data are providing insight into the prognostic significance of characteristics displayed by patients when they first entered the study, as well as the natural history and clinical course of coronary heart disease.

Organization

The study has a policy board of senior nonparticipants which meets annually or more frequently as needed to review the status and results of the study, communicating recommendations from this review to the Director, NHLI. The Steering Committee with Dr. Jeremiah Stamler as chairman meets twice a year. Permanent members are the principal investigators of the original four clinics, senior staff of the coordinating center, and the directors of ECG and central laboratories, as well as (ex-officio) the Chief of Biometrics Research Branch, NHLI, the medical liaison officer and certain other members of NHLI staff. The later clinics are represented on the Steering Committee by three rotating members who are elected by the participating principal investigators for specified terms. The technical group consists of the principal investigators of all clinics and all central facilities. Their semiannual meetings are attended also by medical, administrative, and technical associates. Several other special purpose committees contribute to the operation. They include a Criteria Subcommittee, a Laboratory Subcommittee, and a Statistical Subcommittee (all derived from the Steering Committee); and Editorial Review Board; and a Data and Safety Monitoring Committee. The latter group includes coordinating center staff (who prepare outcome data for periodic review), the chairman of the Steering Committee, the directors of the ECG and central laboratories, five NHLI staff members and two senior physicians, former members of the National Advisory Heart and Lung Council who do not otherwise participate in the study. This body is charged with the important function of searching the data at 3-month intervals for (*a*) untoward or toxic effects which might make it necessary to discontinue the use of any of the drugs; (*b*) a therapeutic effect, relative to placebo; and (*c*) trends of lipid response, adherence levels or dropout rates which might affect accomplisment of the original objectives. Committees on natural history, hepatology and resources have been added within the past year or so.

Status

Fifty-five clinics were recruited in several major metropolitan areas and 36 smaller communities. Two clinics which were unable to recruit the minimum acceptable number of patients were dropped early. Another is being phased out now. The remaining 52 are still active.

From the initially enrolled population of 8,341 patients, there are currently about 6,500 survivors. With an average period of observation of 5 years, all living patients have been followed for at least 4 years and almost two-thirds have passed the 5-year mark. The death rate has been lower than expected, about 4.5 percent each year. The overall dropout rate is only 7 percent, and very few patients have been lost to followup. After dropping both dosage levels of estrogen and dextrothyroxine, evaluation is being continued of three treatment regimens—clofibrate, nicotinic acid, and a lactose placebo. About 2,800 of the original patients were ramdomized to the plabebo group, about 1,100 to each of the active drugs.

Protocol changes

The treatment of patient whose regimens were discontinued was changed to know (to the CDP physician) placebo. Such patients are followed for progression or recurrence of cardiovascular disease at regular clinic visits at least three times a year. A close check on morbidity and mortality is maintained by frequent communications between the CDP physician and those private practitioners who continue to provide general medical care. Laboratory data on these patients show that they gradually reverted to their bochemical baselines. Gynecomastia, a side effect of estrogen, has been much less reversible.

Early in 1973, following recommendations of the Resource Committee, Steering Committee and Policy Board, a double-blind 2-year pilot study on aspirin prophylaxis of nyocardial infarction was undertaken in all clinics, using the otherwise uniformative patients whose original regimens had been discontinued. About 800 potential candidates were available in each treatment group. After screening to eliminate those with aspirin sensitivity, those who would or could not discontinue aspirin therapy which they were already using, those with hemorrhagic disorders (including ulcers) and those unwilling to enter a new trial, nearly 1,200 patients accepted randomization into the aspirin study where they continue to be examined on the regular schedule. Another 550 have been added recently from the low-dose estrogen group.

Findings to date

Three drugs have proved to be ineffective, and have been discontinued. Patients receiving the other two drugs and their placebo controls are still under observation. These medications will be withdrawn this coming summer, and the patients examined one more time during the early winter. The relative merits of the two remaining forms of treatment can then be assessed. Complete analysis of all data will require 2 additional years.

Cost of study

Year-by-year expenses for operation of clinics and support of coordination, statistical analysis, drugs, and research services performed centrally to ensure comparability of results are as follows:

Fiscal year	*Amount*
1965 obligations	$447, 000
1966 obligations	1, 770, 000
1967 obligations	3, 433, 000
1968 obligations	3, 820, 000
1969 obligations	3, 812, 000
1970 obligations	3, 967, 000
1971 obligations	4, 579, 000
1972 obligations	3, 514, 000
1973 obligations	4, 495, 000
1974 estimate	4, 900, 000
1975 estimate	1, 000, 000
1976 estimate	800, 000
Total estimated cost	36, 537, 000

Mr. Flood. Did you want to say something?

Dr. Stone. Yes, sir.

The committee has expressed an interest in PSRO and I wanted to bring to your attention the relationship between the kind of work that is going on in the Heart and Lung Institute and the setting of standards for practice.

I think they are making an extremely important contribution to that whole concept. How PSRO is implemented is another matter, but this development of a data base is enormously valuable in determining how practice will be set up in the future. The actual dollar payoff will be a substantial reduction in the cost of an extensive program.

Mr. FLOOD. You have several of these large clinical trials underway, so you told us.

Dr. COOPER. Yes, sir.

Mr. FLOOD. You develop this for the record, but suppose you describe briefly each one of those trials now.

How much do you have? Give us a fuller statement for the record for each one. Take each one and tell us the whole thing. What I want is something very similar to that multiple risk factor intervention trial which we had printed in last year's hearings beginning on page 327, something like that.

Dr. COOPER. Yes, we will give you a detailed description of its status.

Dr. COOPER. The three main large clinical trials that we have are one in what we call the Lipid Clinics where we will test the lipid hypothesis. These are high risk patients who have very high blood fats of a special type. There will be 4,000 people studied ultimately after the necessary screening is done to test whether a significant lowering of their lipids by a combination of diet therapy and certain kinds of other drugs than we have tested before will in effect prevent or reduce the progression or induce regression of lesions of the coronary arteries.

The second trial is called the multiple risk factor trial in which we will test 12,500 patients who are the upper 10 percent of risk in this country, and the population will be drawn from all over the country, in which they have cigarette smoking, high blood fat, and high blood pressure, and we will test whether a practical regimen of regulating all three will, in fact, do anything for the patient in a free-living setting.

Third, we have a high blood pressure trial in which we are attempting to determine, in a population that is younger than studies that have been done before, including women, blacks, as well as white, and so on, whether these 10,500 patients on appropriate therapy can demonstrate in the absence of symptoms the willingness to stay on the treatment over a long period of time and therefore prevent the catastrophic consequences of high blood pressure, whether it be stroke, heart attack, heart failure, or kidney failure.

We will develop this in great detail with costs for the record.

[The information follows:]

THE LIPID RESEARCH CLINIC PROGRAM—TYPE II CORONARY PRIMARY PREVENTION TRIAL (TYPE II CPPT)

Atherosclerosis and its related disease processes are recognized as major health problems in the developed countries. Over 600,000 deaths from atherosclerotic coronary heart disease occur in the United States yearly. Over 160,000 of these deaths are among men less than 65 years of age. The concept of an attack on atherosclerosis using the Lipid Research Clinics for a collaborative phase IV (human efficacy) primary prevention trial developed from a series of conferences, recommendations, and actions during the years 1970–72.

An expert panel on hyperlipidemia and premature atherosclerosis which convened in June 1970 made recommendations to the National Heart and Lung Institute on ways to achieve the goal of preventing premature atherosclerosis through the diagnosis and treatment of hyperlipidemia. One of these recommendations led to the creation of the lipid metabolism branch in December 1970. Under the branch's aegis, a network of continent-wide Lipid Research Clinics and a Central Patient Registry and Coordinating Center were established whose major objectives included the development of standardized methods and definitions for the diagnosis of hyperlipoproteinemia and the performance of a series of collaborative studies on the prevalence and natural history of these disorders.

A natural progression of this work was the design of a central coordinated, randomized, double-blind. primary prevention trial using patients with hypercholesterolemia. Added impetus for such an undertaking was supplied by several recommendations of a National Heart and Lung Institute task force on arteriosclerosis:

"The task force urges that this program be expanded as expeditiously as possible to include clinical trials of treatment in order to determine whether correction of the blood lipid abnormality by diets and drugs will modify morbidity and mortality from coronary heart disease. It is clear that expansion of the Lipid Research Clinics will also make it possible for them to conduct primary prevention trials in 'high risk' patients and to act as focal points for more elaborate studies on larger populations."

An Intervention Committee was established at the first Lipid Research Clinics directors' meeting in July 1971, to consider program alternatives in intervention. The committee met several times over the subsequent 8 months, and its efforts culminated with the approval of a skeleton intervention protocol by the Lipid Research Clinics Directors and Lipid Metabolism Advisory Committee in May 1972.

In anticipation of a collaborative effort, 12 Lipid Research Clinics were established by November 1972. The final study protocol was approved by the Lipid Research Clinics' directorate in November 1972, with a starting date for patient accrual in July 1973.

OBJECTIVE

The study is designed to test the "Lipid hypothesis"; namely, whether reducing blood cholesterol levels in patients with type II hyperlipoproteinemia can slow down or prevent the development of premature coronary disease.

Type I hyperlipoproteinemia is a common disorder characterized by abnormally high plasma levels of low density lipoprotein, the major carrier of cholesterol, and hence by elevated cholesterol levels. It is strongly associated with premature development of atherosclerosis; the risk of symptoms or death from coronary artery disease ranging from 2.5 to over 10 times that of subjects with normal cholesterol levels. Heart attacks before age 50 are common in type II men.

Although type II hyperlipoproteinemia may be secondary to the consumption of cholesterol-rich diets or to certain other disorders, often it is a hereditary disorder transmitted as a simple Mendelian dominant trait. Thus familial type II occurs with high frequency among the children and other kindred members of affected individuals.

It is now known that the blood cholesterol concentrations of patients with type II can be lowered toward normal through appropriate diets supplemented with the cholesterol-lowering drug cholestyramine. What is not known is whether correction of the blood lipid abnormality results in reduction of the individual's risk of developing symptomatic coronary artery disease such as acute myocardial infarction.

SCREENING

The task of subject recruitment depends on identifying individuals known to have elevated cholesterol levels and who meet other eligibility criteria. The assistance of private and hospital laboratories as well as of established community employee or union medical screening programs is being solicited to help identify potential subjects. Physicians are also invited to refer such subjects. If these methods fail to achieve the intensity of referrals necessary, public recruitment using mass media and community screening may be utilized.

Because of the selection process, a much larger number of potential subjects is necessary in order to obtain the needed 3,600 men required to produce a statistically significant result. It is estimated that some 40,000 individuals will have to be identified and about 10,000 of these actually seen in the clinic to obtain the requisite numbers.

OUTLINE OF STUDY

To be considered for inclusion into the study, subjects must meet the following requirements:

An elevated cholesterol level.

Be men 35–59 years old and likely to remain in the area during the next five years. (For study design reasons, no women will be included in the study.)

Should not have endocrine disease nor severe hypertension.

Should not have angina nor a history of myocardial infarction, congestive heart failure or valvular heart disease.

Should have no known disease that is likely to limit life span to less than 7 years.

All patients who meet these requirements will initially undergo preliminary lipid screening utilizing the standardized core lipid laboratory facilities of the Lipid Research Clinic program. Those found to have type II lipid patterns are then contacted through their physician and undergo further screening to confirm that they meet the initial entrance requirements and are willing to participate in the study. Preliminary evaluation requires five outpatient visits to the Lipid Research Clinic spaced over approximately 5 months. Screening procedures at these visits to be done at no cost to the patient include:

1. Complete blood lipid analyses.
2. Medical and laboratory evaluation including resting and exercise electrocardiography.

All results from the preliminary evaluation are sent to the referring physicians.

TREATMENT PROGRAM

At the fifth clinic visit, patients are randomly assigned to one of two groups. The control group receives the study diet plus a placebo. This diet causes a modest cholesterol reduction. The treatment group receives the study diet plus the choletserol lowering drug cholestyramine. This group will experience a greater reduction in blood cholesterol levels.

The study is double blind so that neither the patients nor the physician knows whether individuals are in the treatment or control group, and no lipid data will be known to the physician after randomization. Cholestyramine has been used for several years with excellent cholesterol lowering in type II patients. Its only common side effect is constipation.

FOLLOWUP

After randomization, participants will be seen at 2-month intervals for the proposed duration of the study for evaluation of study end-points, possible drug toxicity, other disease, and adherence to treatment.

END-POINT

It is postulated that cholesterol reduction with cholestyramine will produce a significant decrease in the death rate from atherosclerotic coronary heart disease and in the occurrence rate of definite nonfatal myocardial infarction in group of asymptomatic patients with primary type II hyperlipoproteinemia, also receiving a cholesterol lowering diet, when compared with a diet and placebo treated group.

Study participants will be followed for 7 years unless the data demonstrate earlier that correction of the lipid abnormality in type II favorably alters the course of patients and reduces the threat of acute heart attacks and other sequelae.

For the protection of participants, a separate Safety and Data Monitoring Board will periodically review the results.

An Intervention Committee is responible for the design and operational planning for detailed procedures carried out at each clinic on a standardized basis. Patient data is recorded on standard forms and submitted to the Central Patient Registry and Coordinating Center of the program for biostatistical analysis. Regular reports on trial progress are submitted to the Safety and Data Monitoring Committee.

GENERAL SIGNIFICANCE

Although only a portion of total atherosclerotic coronary heart disease rate occurs in patients with hypercholesterolemia in the general population, the use of the high-risk type I population provides the means to answer an urgent problem in as short a time as possible with the resources available. There is evidence that, in younger men, type II may be important in the occurrence of premature atherosclerotic coronary heart disease. Moreover, if, as strongly suggested by several prospective studies, cholesterol and atherosclerotic coronary heart disease risk are relater over the entire range of cholesterol, then a positive result in a subgroup that represent the top part of the distribution should have positive implications for the whole cholesterol range.

Such evidence indicates that positive findings from this study will be a powerful addition in support of the lipid hypothesis.

PARTICIPATING INSTITUTIONS

The participating clinical centers and principal investigators in the lipid research clinic program are:

Peter O. Kwiterovich, M.D., Johns Hopkins University, Baltimore, Md.

Antonio M. Gotto, M.D., Baylor College of Medicine, the Methodist Hospital, Houston, Tex.

William R. Hazzard, M.D., University of Washington, Seattle, Wash.

W. Virgil Brown, M.D., Daniel Steinberg. M.D., University of California, San Diego, La Jolla, Calif.

John W. Farquhar, M.D., Leland Stanford Junior University, Stanford, Calif.

J. Alick Little, M.D., University of Toronto, Toronto, Ontario, Canada.

Ivan D. Frantz, Jr., M.D., University of Minnesota, Minneapolis, Minn.

William E. Connor, M.D., Francois Abboud, M.D., University of Iowa, Iowa City, Iowa.

Charles J. Glueck, M.D., University of Cincinnati, Cincinnati, Ohio.

Reagan H. Bradford, M.D., Oklahoma Medical Research Foundation, Oklahoma City, Okla.

Gustav Schonfeld, M.D., Washington University, St. Louis, Mo.

John LaRosa, M.D., George Washington University, Washington, D.C.

Cooperating nonclinical centers are:

James E. Grizzle, Ph. D., Central Patient Registry, University of North Carolina, Chapel Hill, N.C.

L. Thomas Sheffield, M.D., Central Exercise Laboratory, University of Alabama, Birmingham, Ala.

Gerald Cooper, M.D., Lipid Standardization Center, Center for Disease Control, Atlanta, Ga.

Central Clinical Chemistry Lab, Bio-Science Laboratories, Van Nuys, Calif.

Drug Supply and Distribution Center, Mead Johnson & Co., Evansville, Ind.

The Chairman and members of the Safety and Data Monitoring Committee are as follows:

Robert I. Levy, M.D. (Chairman), Director, Division of Heart and Vascular Diseases, National Heart and Lung Institute, Bethesda, Md.

Harold Fallon, M.D., chief of medicine, Medical College of Virginia, Richmond, Va.

Clarence E. Davis, Ph. D., Department of Biostatistics, School of Public Health, University of North Carolina, Chapel Hill, N.C.

James Grizzle, Ph. D., chief, Department of Biostatistics, School of Public Health, University of North Carolina, Chapel Hill, N.C.

Herman A. Tyroler, M.D., professor of epidemiology, School of Public Health, University of North Carolina, Chapel Hill, N.C.

Henry McGill, Jr., M.D., Department of Pathology, University of Texas, San Antonio, Tex.

Proctor Harvey, M.D., professor of medicine, Georgetown University School of Medicine, Washington, D.C.

William T. Friedewald, M.D., chief, Clinical Trials Branch, DHVD, National Heart and Lung Institute, Bethesda, Md.

ESTIMATED COST

The total Lipid Research Clinic program budget from its inception until the projected conclusion of its clinical trial component will be $103.5 million. Of this, approximately one-third specifically covers the clinical trial costs; an additional 15–30 percent relates to Lipid Clinic resources (core lipid and exercise laboratories) which perform clinical trial and other progammatic measurements. The remaining 40–55 percent of the total funds relate to Lipid Research Clinic program activities other than the type II coronary primary prevention trial. The objectives of these new clinical trial activities include:

1. Establishment and maintenance of core laboratories capable of accurate quantitative measurements of plasma lipids and lipoproteins.
2. Conducts studies to define the prevalence of the different types of familial and sporadic hyperlipoproteinemia and their coexistence with coronary vascular disease.
3. Establishment of each Lipid Research Clinic as a regional resource and reference laboratory for lipid and lipoprotein methodology and as a dietary and clinical consultation service for patients, physicians, dietitians and nures.
4. Evaluation of current techniques for the diagnosis of hyperlipoproteinemia and the development of better ones.
5. Development and evaluation of methods for dietary counseling, evaluation and monitoring.
6. Establishment of clinic faciilties in which both children and adults with hyperlipoproteinemia can be detected, evaluated and treated while the family is followed as a unit.
7. Development in all clinics of standardized cardiac exercise laboratories capable of performing and analyzing up to thirty exercise tolerance tests weekly.

Total lipid clinic program

[Dollars in millions*]

Summary of projected costs	
Fiscal year:	
1971, 6 clinics and coordinating center	2.5
1972, additional 6 clinics, protocol development	5.4
1973, patient recruitment commenced	8.3
1974, recruitment and observation	10.3
1975, observation	11.0
1976, observation	11.0
1977, observation	11.0
1978, observation	11.0
1979, observation	11.0
1980, observation	11.0
1981, conclusion of trial, data analysis	11.0
Total	103.5

*Approximately 45 to 60 percent of total lipid research clinic program cost is devoted to the clinical trial; the balance relates to other collaborative studies (prevalence, nutrition, exercice electrocardiography, family studies, and cord blood studies) and to relevant noncollaborative research.

THE MULTIPLE RISK FACTOR INTERVENTION TRIAL (MRFIT)

Research findings from well conducted prospective epidemiological studies in a number of populations in the United States over the past 20 years have convincingly established that elevated blood cholesterol, elevated blood pressure and cigarette smoking are risk factors associated with accelerated development of myocardial infarction, sudden death and death from coronary heart disease. These are not the only risk factors associated with premature development of CHD but these factors are modifiable and provide a strong expectation that a reduction of these factors should have a beneficial result of reducing the rate of development of premature heart attacks.

Thorough consideration of scientific knowledge relating to the established risk factors in coronary heart disease by the NHLI Task Force on Arteriosclerosis resulted in the following recommendation:

> Multifactor Prevention Trials. In addition to clinical trials in which treatment is directed toward a single risk factor, trials can be undertaken where treatment is directed simultaneously toward a number of risk factors. Such combined intervention more closely resembles the type of intervention that would be carried out by a physician in his treatment of a patient.

> The task force recommends that the National Heart and Lung Institute undertake multiple risk factor intervention trials in individuals at high risk because of combinations of elevated serum lipids, hypertension, and cigarette smoking. These trials will have the merit of demonstrating whether or not intervention can prevent the complications of human arteriosclerosis since this is the crucial question as yet unanswered by direct experiment. These trials would not delineate the effects of the various individual risk factors.
>
> The task force reviewed this question and convened a panel of experts to consider such trials. It was concluded that such trials would be feasible. These trials would require populations of manageable size and would be likely to yield a meaningful answer. Similar studies are also in various stages of planning or in operation in European countries under the auspices of the World Health Organization.

The Institute has accepted the need to determine in a scientifically designed clinical trial whether or not a preventive program directed at the reduction of elevated serum lipids, elevated blood pressure and cigarette smoking in men between the ages of 35–57 can achieve a significant reduction in heart attacks and death from coronary disease.

OBJECTIVES

To determine whether or not a preventive program directed at the reduction of serum cholesterol, reduction of blood pressure, and reduction or elimination of cigarette smoking among men aged 35–57, who are at high risk of coronary heart disease from a combination of these risk factors can result in a significant reduction in the incidence of myocardial infarcation and death from coronary heart disease over a 6-year primary intervention clinical trial.

PRIMARY SCREENING

It is estimated that each center, to obtain 600 eligible high-risk volunteers, will need to screen 12,000–20,000 men initially unless access is available to recently screened populations in which adequately performed blood pressure, cholesterol measurements, and smoking history allow classification. Men from the general population who have known elevation of blood pressure or elevated blood lipids can also be invited for screening to determine eligibility providing that they are not already under drug or medical regimens for these risk factors. A total study population of 12,000 participants will be sought for participation in this prevention program for a period of 6 years.

RANDOMIZATION

Fifty percent of those volunteering to the program and having obtained approval of their physician to participate will be randomized to the special intervention program. The others will be referred to their physicians or their usual source for care and invited to return to the clinic on an annual basis for repeat examinations including height-weight, blood pressure, blood lipids, and electrocardiogram.

INTERVENTION PROGRAMS

The purpose of this program is to intervene on each of the elevated risk factors present in the subjects randomized to the study group—effecting specifically at least a 10-percent reduction of cholesterol level, 10 percent reduction of diastolic blood pressure level, and reduction or discontinuation of cigarette smoking.

Emphasis in the nutrition program will be directed toward changes in food habits compatible with the characteristics of a free-living population. The lipid-lowering diet will be taught as a change in food choices regarding the major food groups that contribute most of the saturated fat and cholesterol to the diet. The concept of the development of new food choices and food patterns will be promoted; highly structured diets will be avoided. All participants will be given the same basic instruction, but it will be adapted to their special needs due to literacy, type of learner, ethnic food patterns, and economic considerations.

The program goal for intervention on hypertension is to reduce diastolic blood pressure 10 percent on the average. From a clinical standpoint, the goal will be to reduce diastolic blood pressure to 90 mm Hg or 10 mm Hg below baseline, whichever is lower. This goal for individuals will be pursued via weight reduction where appropriate and/or standard drug regimens to the degree tolerated by the patient with regard to side effects.

The goal of this intervention modality is to reduce the average daily cigarette consumption by at least 50 percent for the study group. For individuals, the goal will vary from almost immediate complete cessation of smoking to stepwise reduction, temporary substitution of cigars or pipes (or low-caloric, low-fat snacks) with recognition and support of week-by-week or month-by-month goal attainments.

FOLLOWUP

There will be systematic surveillance at similar intervals for both study and control groups to determine hospitalizations or diagnosis of major clinical events (e.g. myocardial infarctions, strokes, deaths). Systematic followup of the study group will occur at intervals of approximately 2 months (more frequently initially) with designed and documented incremental effort applied to reduce dropouts and poor adherers.

LOGISTICS

This clinical trial requiring 12,000 volunteer participants will be conducted under direct supervision of professional medical, nutritional and biostatistics staff of the Institute who will be working directly with the selected investigators to plan the detailed procedures for all aspects of this planned 6 year prevention trail.

Twenty clinical centers each enrolling 600 participants have been selected. In addition a statistical coordinating center, a central laboratory and an electrocardiography center and a Drug Distribution Center complete the necessary teams needed for conduct of this study.

A steering committee representing the selected principal investigators provides operational planning for detailed procedures to be carried out in each center on a standardized basis.

A Policy Advisory Board has been established to provide independent scientific review and monitoring throughout the course of the trial. The Policy Advisory Board must recommend on all procedures which will be incorporated into the trial, including the acceptability of the scientific design, the operational feasibility, the nature of the intervention regimens, and the system for monitoring possible side effects. The Board also advises on ethical aspects in relation to NHLI and Government policies relating to programs involving research on human subjects.

The planning phase and pilot testing phase were completed by November 1973. Enrollment of the 12,000 participants is proceeding and should be completed in 1975. Participants will be maintained under the planned prevention program for a 6-year period of followup.

All clinical events of coronary heart disease will be recorded in both the intervention group as well as in the control group including special annual cardiovascular measurements to detect silent coronary disease over this period. Statistical monitoring will be made of these rates in the two groups to determine the degree of benefit which may result from reduction of these risk factors.

PARTICIPATING INSTITUTIONS

The participating clinical centers, and principal investigators in the MRFIT are as follows:

University of Maryland, Baltimore, Md., Maureen Henderson, M.D.; Roger Sherwin, M.D.

University of Minnesota, Minneapolis, Minn., Henry Blackburn, M.D.; Henry Taylor, Ph. D.

St. Louis Heart Association, St. Louis, Mo., Herbert Zimmerman, M.D.

Harvard University, Boston, Mass., James E. Dalen, M.D.

Kaiser Foundation Resident Institute, Portland, Oreg., John Wild, M.D.; John Grover, M.D.

Cox Heart Institute, Kettering, Ohio, Paul Kezdi, M.D.

Lankenau Hospital, Philadelphia, Pa., William Holmes, Ph. D.; J. Edward Pickering, M.D.

University of Pittsburgh, Pittsburgh, Pa., Lewis Kuller, M.D.; Robert McDonald, Jr., M.D.

University of Southern California, Los Angeles, Calif., Jessie Marmorston, M.D.

Rutgers Medical School, Piscataway, N.J., Marise Gottlieb, M.D.

American Health Foundation, New York, N.Y., Peter Peacock, M.D.; Ernest Wynder, M.D.

American Health Foundation, New York, N.Y., Peter Peacock, M.D.; Ernest Wynder, M.D.

Pacific Medical Center, San Francisco, Calif., Stephen Hulley, M.D.; W. McFate Smith, M.D.

University of California, Davis, Calif., Nemat Borhami, M.D.; Dean Mason, M.D.

Northwestern University, Chicago, Ill., Jeremiah Stamler, M.D.; Oglesby Paul, M.D.

Boston University, Boston, Mass., Thomas Dawber, M.D.; H. Emerson Thomas, M.D.

New Jersey Medical School, Newark, N.J., Norman Lasser, M.D., Ph. D.

University of Alabama, Birmingham, Ala., Harold Schnaper, M.D.; Hugh Pratt, M.D.

University of South Carolina, Columbia, S.C., Warren Giese, Ph. D.; Robert Kiger, M.D.

Dade County Department of Public Health, Miami, Fla., Milton Saslaw, M.D.; Janice Burr, M.D.

Rush Medical College, Chicago, Ill., James Schoenberger, M.D.; Milton Levine, M.D.

Cooperating nonclinical centers are:

Coordinating Center, University of Minnesota, Minneapolis, Minn., Marcus Kjelsberg, Ph. D.

Electrocardiographic Center, University of Dalhousie, Halifax, Nova Scotia, Penta Rautaharju, M.D., Ph. D.; Hermann Wolf, M.D.

Lipid Standardization Center, Center for Disease Control, Atlanta, Ga., Gerald Cooper, M.D.; Myron Kuchman, M.D.

Central Laboratory, Pacific Medical Center, San Francisco, Calif., Graham Widdowson, Ph. D.; George Z. Williams, M.D.

Electrocardiographic Coding Center, University of Minnesota, Minneapolis, Minn., Ronald Prineas, M.D.

Drug Distribution Center, USPHS Supply Center, Perry Point, Md., Mr. Salvatore Gasdia.

The Chairman and members of the Policy Advisory Board are as follows:

John Cassel, M.D.—chairman, Head, Department of Epidemiology, University of North Carolina, Chapel Hill, N.C.

Harriet P. Dustan, M.D., vice chairman, Research Division, Cleveland Clinic, Cleveland, Ohio.

William Insull, Jr., M.D., adjunct associate professor and physician, Center for Prevention of Premature Arteriosclerosis, Rockefeller University, New York, N.Y.

C. David Jenkins, Ph. D., professor, Department of Behavioral Epidemiology, Division of Psychiatry, Boston University School of Medicine, Boston, Mass.

Donovan J. Thompson, Ph. D., professor of biostatistics, Department of Preventive Medicine, University of Washington, Seattle, Wash.

Charlotte M. Young, Ph. D., professor of medical nutrition, Cornell University, Ithaca, N.Y.

William J. Zukel, M.D. (ex officio), associate director for clinical applications and prevention, Division of Heart and Vascular Diseases, National Heart and Lung Institute, Bethesda, Md.

ESTIMATED COST

The estimated total cost of this study from its beginning planning stage, population screening and enrollment of 12,000 participants for 6 years of subsequent followup including final data analysis, will be approximately $98 million.

Summary of Projected Costs

	Millions
Fiscal year 1972 8 centers planning and pilot testing procedures	$3.2
Fiscal year 1973 15 centers screening and beginning enrollment phase	[1] 8.7
Fiscal year 1974 20 centers screening and enrollment	11.2
Fiscal year 1975 20 centers intervention phase	10.4
Fiscal year 1976 20 centers intervention phase	11.0
Fiscal year 1977 20 centers intervention phase	11.4
Fiscal year 1978 20 centers intervention phase	11.5
Fiscal year 1979 20 centers intervention phase	12.0
Fiscal year 1980 20 centers intervention phase	12.4
Fiscal year 1981 Completion of intervention, data analysis	6.4
Total	98.2

[1] Due to delay of screening, the actual funding level was $7,200,000. This deferred amount ($1,500,000) is anticipated to be required for the subsequent operating year.

NHLI HYPERTENSION DETECTION AND FOLLOWUP PROGRAM (HDFP)

GENERAL BACKGROUND AND RATIONALE

Treatment of elevated blood pressure constitutes one of the most important challenges to chronic disease control in the United States at the present time. This is true in regard to all segments of the adult population—young, middle-aged, and elderly, male and female, affluent and impoverished, white and black.

Recent studies have defined the challenge represented by elevated blood pressure:

1. There are an estimated 23 million persons with high blood pressure in the United States. These people though usually initially symptom free are at significant risk of progression into a higher morbidity, disability and premature death from associated complications such as stroke, heart disease, and renal failure.
2. The health and longevity of the public with high blood pressure is significantly reduced, not only in persons with marked elevations of blood pressure but also for those in the much larger group with diastolic blood pressures in the 90 to 104 mm Hg range. Many physicians may yet be unaware or not give appropriate weight to the significance of the finding of mildly elevated blood pressure in their patients.
3. Prevalence rates and mortality data indicate high blood pressure to be a proportionately more severe problem among economically poor people and particularly black people. The problem among black people is unusually severe in the young adult age group.
4. A substantial proportion of individuals with elevated blood pressure in the American population are unaware that they harbor this condition and a sizable proportion of known hypertensives are not being treated on a continuing basis.
5. When hypertension is present along with other prognostically important findings (e.g., cigarette smoking), the risk of mortality and morbidity rise markedly.

The challenge of the high blood pressure problem is even more pressing since it is likely that technology of treatment control is presently available. Possibly the most convincing evidence available to date in this regard is the Veterans' Administration study which was reported in 1970. This study confirmed that defined combinations of drug therapy were effective in reducing high blood pressure and that this therapy was effective in reducing the rate of nonfatal and fatal complications even in men with mild high blood pressure. Direct extrapolation of the therapeutic implications of the results of the Veterans' Administration study to all persons with high blood pressure in the United States is somewhat limited by the characteristics of that study which was conducted in a middle-age and elderly group of male subjects who had been selected by criteria related to blood pressure levels during hospitalization and to the likelihood of compliance to the regimen.

This background of high blood control knowledge contributed to the meeting of an ad hoc panel at NHLI in the fall of 1970 to review current data in hypertension trials. This panel recommended:

"The first priority need is to determine the effectiveness of antihypertensive therapy in reducing morbidity and mortality from hypertension in the general population. Such studies should include both sexes, all races in a community, and preferably younger as well as middle-age ranges. Such a study would not have a placebo group but could allow randomization of subjects for comparison of optimum drug regimens versus the customary medical care in the community. Pilot studies and feasibility studies in general populations and in special communities should be undertaken to quantitate the applicability of current or innovative methods of management of hypertension."

The hypertension detection and followup program was begun in 1971 to address itself directly to these challenges. Fourteen clinical centers, one coordinating center, and a central laboratory were selected from the competition of responses to RFP's issued by NHLI. The program has combined aspects of two basic approaches—a classical clinical trial and a community public health effort—in a manner appropriate to the present transitional situation in regard to knowledge concerning the ability to manage the massive hypertension problem. The purpose of the hypertension detection and followup program is to determine the effectiveness of a systematic approach of antihypertensive therapy in those with elevated blood pressure in representative community-based populations across the United States.

SPECIFIC AIMS

In this national cooperative multicenter effort, involving a broad and varied spectrum of persons with hypertension identified in representative communities across the United States, the hypertension detection and followup program aims to:

1. Assess the ability of a stepped care program (versus regular care) of long-term antihypertensive therapy and appropriate medical management to reduce mortality, disability and morbidity associated with elevated blood pressure and thereby increase life expectancy and quality of life. Mortality from all causes is the primary endpoint. It is anticipated it will be necessary to follow a group of 10,500–11,000 hypertensive individuals randomly divided into stepped care and regular care for 5 years.

Secondary endpoints include cause specific mortality as well as nonfatal myocardial infarction, stroke, congestive heart failure, malignant hypertension, ischemic heart disease (ECG), cardiac enlargement on chest X-ray, left ventricular hypertrophy (ECG), and renal failure (abnormal serum creatinine) when evident at annual and/or biennial examination (see sec. D).

2. Assess the effects of this stepped care program (versus regular care) on key intermediate measurements related to risk of major clinical cardiovascular complications in hypertensive patients—e.g., systolic and diastolic blood pressure, serum creatinine, plasma glucose, serum uric acid, resting electrocardiogram and heart size on PA chest X-ray.

3. Monitor and evaluate the side and toxic effects of antihypertensive medication of the stepped care program.

4. Estimate the ability of the stepped care program to influence life expectancy in the total age-eligible population enumerated, using mortality from all causes as the endpoint.

5. Enhance and evaluate means for achieving effective therapy of hypertension in various socioeconomic, ethnic and racial strata of the United States. This will include assessment of performance of health manpower, methods of organization and administration of hypertension control facilities, education of professional staff, and health education and medical care contact with participants.

ENDPOINTS

The endpoints to be used in evaluation of this program are those which can be clearly ascertainable from data of annual and/or biennial examinations of the regular care and stepped care groups, from annual mortality surveillance to be done on all hypertensive persons, and from a sample of the entire screened population in each center.

Following an NHLI study in 1971 and 1972 of the feasibility of such large-scale screenings, standardized screening began in February 1973, and by March 15, 1974, 157,128 individuals were screened. Each community clinical center is doing this primary screening in the homes (or at work in one center). Of the adults aged 30–69 identified in the household enumeration, individuals with elevated diastolic blood pressure (≧95 mm Hg) have been invited to the clinic for recheck of their blood pressure. If the average diastolic blood pressure taken at the clinic is also elevated ≧90 mm Hg, a baseline workup including medical history, physical examination, routine laboratory tests, an electrocardiogram and a chest X-ray is done. The intake of approximately 11,000 hypertensive participants will be completed in April. First year followup has already begun in the regular care as well as the stepped care groups.

Of the persons identified, confirmed at followup screening clinics to have elevated diastolic blood pressure, and invited to participate in the program, 50 percent are in the stepped care group. They are receiving energetic care by program staff. Stepped care refers to the plan of therapy in which mild antihypertensive agents are initially prescribed, and more potent agents added, if necessary, in a defined stepwise manner until the goal blood pressure or as close to goal pressure as is tolerated is reached. Goal blood pressure is defined as either 90 mm Hg diastolic or below or a reduction of 10 mm Hg below baseline whichever is lower.

While the program is designed expressly to evaluate antihypertensive care at the community level, it is necessary also to standardize certain other aspects of clinical management in conformity with present standards of good medical care. Because smoking, elevated serum cholesterol levels and obesity all are cardiovascular risk factors and relate to morbidity and mortality, a standardized approach to giving advice on reducing risk from these factors is prescribed. A uniform set of diagnostic procedures is used to seek out individuals with secondary hypertension among those confirmed to have elevated blood pressure. Further diagnostic evaluations for causes of secondary hypertension are being undertaken in clinically suspect participants in the stepped care group. Side effects and toxicity will be monitored and necessary corrective measures will be taken according to procedures in the manual of operations. If these untoward events become too frequent in a specified portion of the stepped care group, necessary action to modify the protocol as may be recommended by the toxicity and endpoints evaluation committee and approved by the steering committee and the policy advisory board will be undertaken.

In summary, approximately 23 million Americans have high blood pressure, the vast majority are undetected, untreated or not effectively controlled. There is a growing national concern about this problem. This hypertension detection and followup program is one effort to deal with some of the many problems that need to be solved as we all work toward meeting this critical public health challenge.

ESTIMATED COST

The estimated total cost of the hypertension detection and followup program contracts including pilot and feasibility studies, screening of 160,000 persons to obtain 10,500 to 11,000 hypertensive participants and 5 years of followup plus a year of final data analysis is $60.32 million.

Fiscal year	Amount (millions)	Item
1971	$2.20	Pilot studies and feasibility study.
1972	4.00	
1973	6.10	Beginning of recruitment.
1974	8.30	Completion of recruitment.
1975	7.66	5 yr of follow-up and data analysis.
1976	7.80	
1977	8.23	
1978	8.64	
1979	6.89	
1980	.50	Data analysis.
Total	60.32	

HYPERTENSION DETECTION AND FOLLOW-UP PROGRAM CENTERS

A listing of the centers which have been awarded contracts is provided below:

Reuben Berman, M.D., Mount Sinai Hospital, Minneapolis, Minn.

M. Donald Blaufox, M.D., Ph. D., and Bertrand Bell, M.D., Albert Einstein College of Medicine, Yeshiva University, Bronx, N.Y.

Nemat O. Borhani, M.D., University of California, Davis, Calif.

C. Hilmon Castle, M.D., and Alex Kralois, M.D., University of Utah Medical Center, Salt Lake City, Utah.

Sandra A. Daugherty, M.D., Ph. D., Michigan State University, East Lansing, Mich.

George Entwisle, M.D., and Maureen Henderson, M.D., University of Maryland Hospital, Baltimore, Md.

Frank A. Finnerty, Jr., M.D., Georgetown University, Washington, D.C.

Curtis G. Hames, M.D., and Iqbal Krishan, M.D., Evans County Health Department, Claxton, Ga.

Edward Kass, M.D., and James O. Taylor, M.D., Boston City Hospital, Boston, Mass.

Herbert Langford, M.D., University of Mississippi Medical Center, Jackson, Miss.

Morton Maxwell, M.D., Cedars-Sinai Medical Center, Los Angeles, Calif.

Harold W. Schnaper, M.D., and Albert Oberman, M.D., University of Alabama Medical Center, Birmingham, Ala.

Jeremiah Stamler, M.D., Northwestern University Medical School, Chicago, Ill.

Elbert P. Tuttle, Jr., M.D., Emory University School of Medicine, Atlanta, Ga.

Richard Remington, Ph. D., and C. Morton Hawkins, Sc. D., University of Texas (HDFP Coordinating Center), Houston, Tex.

Kenneth A. Schneider, M.D., Northwestern Memorial Hospital (HDFP Central Laboratory), Chicago, Ill.

Ronald Prineas, M.D., University of Minnesota (HDFP ECG Center), Minneapolis, Minn.

HDFP POLICY ADVISORY BOARD

The Hypertension Detection and Follow-Up Program Policy Advisory Board members are:

Alvin P. Shapiro, M.D., chairman, Professor of Medicine, University of Pittsburgh School of Medicine, Pittsburgh, Pa. 15213.

Glenn E. Bartsch, Ph. D., Biometry Division, University of Minnesota School of Public Health, Minneapolis, Minn. 55455.

Kenneth G. Berge, M.D., Consultant in Medicine, Mayo Clinic, East 8, Rochester, Minn. 55901.

Edward D. Frolich, M.D., Professor of Medicine, Health Sciences Center, University of Oklahoma, Oklahoma City, Okla. 73104.

Richard H. Gadsden, Ph. D., Professor of Biochemistry and Clinical Pathology, Medical University of South Carolina, S.C. 29401.

Edward Hawthorne, M.D., Head, Department of Physiology and Biophysics, Howard University College of Medicine, Washington, D.C. 20001.

David L. Sackett, M.D., Department of Clinical Epidemiology and Biostatistics, McMaster University Medical Center, Hamilton 16, Ontario, Canada.

Joseph A. Wilber, M.D., Director, Cardiovascular Disease Control Service, Georgia Department of Public Health, Atlanta, Ga. 30334.

INTRAMURAL RESEARCH

Mr. Flood. Your budget includes 345 jobs for intramural laboratory and clinical research. Do you think the intramural research program of your particular institute should be expanded beyond that level? How much?

Dr. Cooper. We feel that the intramural research program is a very important, integral part of our total plan. We feel, for example, the contribution that has been made to the total concept of developing the test of the lipid hypothesis, the multiple risk factor trial, in large part eminated from the laboratories at Bethesda.

Therefore, the ability to lead that work from our own laboratories at Bethesda was an invaluable resource to us and probably the most efficient way to do it. That was in the lipid question.

We have also had in the past the opportunity to have expert studies going on in high blood pressure right there at the Bethesda area. This has also allowed us the ability to develop and implement plans at a much more rapid and efficient pace than if we did not have them.

The areas which we would like to implement further by redesigning our efforts with what resources are available in manpower and space are in implementing a series of similarly distinguished laboratories in the lung and in what we call molecular hematology to undergird our programs that we are responsible for in blood and blood banking.

So we do feel that our intramural program is very essential to our total concept and indeed we would like to insure its stability and validity.

EMPHYSEMA

Mr. Flood. Are you making any significant progress at all on either the prevention or the treament of emphysema?

Dr. Cooper. Yes, sir; I think we are. I think the things we are learning about emphysema that are important are these: First, we have devised——

Mr. Flood. In my part of the country a great awareness has developed because of the awareness of the black lung problem.

Dr. Cooper. I think there is very exciting activity going on in the field of chronic lung disease. I think we have new techniques for detecting the early emphysematous patient.

Mr. Flool. I don't mean that black lung is emphysema.

Dr. Cooper. But it would apply to the same thing. I think you are absolutely correct. I think the early detection of pulmonary incapacity has long been ignored and I think we have newer measurements clinically that will allow us to detect the patient earlier.

Second, we have been able by applying basic technology, molecular biology, and cystology, to the lung which had not been done before also to determine that the lung is made up of several different kinds of cells and we are now able to identify which cells react to which type of noxious injury.

We know which ones make collagen. The collagen is the scar tissue in the lung. Emphysema is caused by destruction of the normal lung tissue by the scar tissue when certain injurious agents come in. This ability to study the lung at a fundamental level is a real advance.

In adition, we are able by new epidemiology studies to identify people at risk by virtue of some genetic, perhaps deficiencies of enzymes in their system which might make their lung tissue less responsive to healing in a normal way.

Mr. Flood. Is cigarette smoking the chief cause of emphysema?

Dr. Cooper. On a correlated basis it is quite true that people with emphysema smoke more frequently than people who do not, but I would not call that necessarily a cause and effect response.

Mr. Flood. What would you say about the Government's efforts? Would you say the Government's effort to persuade people not to smoke has been pretty largely ineffective?

Dr. Cooper. No; I would say that it depends on what you want to use as the yardstick and how you want to measure it. The fact is many people, particularly doctors, 100,000, are said to have stopped smoking. The question asked, I think, is, suppose you didn't have the effort? How many would be smoking then? I think the next question is, Are you willing to expend the same amount of money to combat smoking as the people who promote smoking.

I think that is a different kind of a question.

Mr. Flood. Let us talk about something else.

FELLOWSHIP AND TRAINING GRANT PROGRAM

The budget proposes an expansion of the fellowship program and a phaseout of the training grant program. Does that policy make sense in your judgment? You have a bear by the tail there.

Dr. Cooper. Yes, I have a bear by the tail here.

Let me see if I can say this without getting hit on the head.

I think that research, the development of research manpower, is necessary. I think the question that has been at debate is what is the Federal role in that, and the philosophical approach as to whether or not the individual trainee should seek out the place that he wants or whether the selection is best made in areas in which the environment can better select it because the young trainee in effect has no track record. There is very little data at that level to say either approach is necessary. My own philosophy is that it is not an either/or philosophy. I personally feel that the yielding of any capability of any mechanism reduces flexibility to attract young people into the field and my own preference if national priorities and policy permitted would be to have both.

If they do not, then I would think we would have to try to make best utilization with the capabilities we have.

Mr. Flood. Do you believe we have enough young people who are qualified to do this research in heart, blood vessel, and lung, blood diseases? Take a look at page 82 of your justifications there. That is what prompts this:

> A common problem potentially threatening all these trials is limited availability of adequate expertise to carry out multiclinic trials as well as a limited supply of acceptable study patients.

Dr. Cooper. The answer to your question is, "Yes," I think we do need additional personnel. If there is going to be an expanded national effort in this area I think the manpower base for its execution must be commensurate with the size of the commitment.

Mr. Flood. For the record then let us have a table showing the number of trainees and fellows supported from this appropriation in 1973, 1974, and for 1975.

Dr. Cooper. We have such data. We will submit it.

[The information follows:]

NATIONAL HEART AND LUNG INSTITUTE—ESTIMATED NUMBER OF FELLOWS AND TRAINEES FUNDED IN 1973, 1974, AND 1975

	1973	1974	1975
Fellows	100	400	660
Trainees	1,470	675	225

Mr. FLOOD. Your justification also says, and this I quote again:

> Assistance to graduate students in the life and social sciences will be more equitably provided under the expanded general assistance programs available to all graduate students through the Office of Education.

For the record after all that, naturally I want a listing of the programs, the estimates of the amount expected to be available to the graduate students through these programs through fiscal year 1975. You can do that?

Dr. COOPER. Yes, sir.

[The information follows:]

OFFICE OF EDUCATION—HIGHER EDUCATION

The primary program offering assistance to graduate students in the Office of Education is in the appropriation relating to higher education. In 1975, $315 million will be available for loan subsidies in the guaranteed student loan program. Page 112 of the budget proposed for the Department of Health, Education, and Welfare, for the fiscal year ending June 30, 1975, reads, "The guaranteed student loan program, with the infusion of additional private capital generated by the Student Loan Marketing Association, will make available more than $1 billion of student loans annually to about 1 million students. Legislation will be proposed to increase the present $10,000 ceiling on guaranteed loans to a new level of $25,000 to provide for professional or other graduate education."

The National Heart and Lung Institute has traditionally supported research programs—and research training programs—in the life sciences. These programs have mostly relied on manpower developed in the Nation's medical schools and graduate schools in the life and physical sciences. With the mandate of the Institute broadened by Public Law 92–423, particularly with reference to national research and demonstration centers and for prevention, education, and control programs, the Institute will need to draw more and more upon other educational sources for programs which will include, as well as physicians and scientists, professional managers and administrators, engineers, social workers, nurses, and educators.

OBLIGATIONS OF RESTORED 1973 FUNDS

Mr. FLOOD. You are obligating $44,103,000 in fiscal 1974 from funds appropriated in fiscal year 1973. For the record again we want a breakdown of that amount, a statement of how these funds are being used.

Dr. COOPER. Yes, sir.

[The information follows:]

NATIONAL HEART AND LUNG INSTITUTE

DISTRIBUTION OF 1973 IMPOUNDED FUNDS

[Amounts in thousands of dollars]

Budget mechanism	Number of awards	Amount
Research grants, regular:		
Heart and vascular diseases	27	2,900
Lung diseases	6	648
Blood diseases and resources	6	648
Total	39	4,196
Research grants, special research career program:		
Heart and vascular diseases	69	1,730
Lung diseases	9	225
Blood diseases and resources	11	276
Total	89	2,231
Fellowships:		
Heart and vascular diseases	22	317
Lung diseases	3	38
Blood diseases and resources	3	39
Total	28	394
Training grants:		
Heart and vascular diseases	18	3,152
Lung diseases	6	950
Blood diseases and resources	1	216
Total	25	4,318
Research and development contracts:		
Heart and vascular diseases	40	22,300
Lung diseases	60	4,800
Blood diseases and resources	60	4,797
Total	160	31,897

MULTIPLE-YEAR GRANTS

Mr. FLOOD. How much money are you obligating in fiscal 1974 for this multiple-year funding—that is, that 2 years or more business—of grants or contracts and give us a breakdown of that amount which would show how much is being obligated for use in the subsequent years.

We want that for the record.

Dr. COOPER. Yes.

[The information follows:]

MULTIYEAR FUNDING FROM 1974 APPROPRIATION	Number of awards	Total amount	Amount affecting 1975 funding
Research grants:			
Heart and vascular diseases	5	416	208
Lung diseases	52	2,349	1,104
Blood diseases and resources	2	208	104
Fellowships:			
Heart and vascular diseases	13	420	210
Lung diseases	2	90	45
Blood diseases and resources	2	90	45
Training grants:			
Heart and vascular diseases	15	3,084	2,453
Lung diseases	4	930	739
Blood diseases and resources	1	211	168
Research and development contracts: Heart and vascular diseases	53	12,602	5,600
Totals:			
Heart and vascular diseases	86	16,522	8,471
Lung diseases	58	3,369	1,888
Blood diseases and resources	5	509	317
Total	149	20,400	10,676

	Number of awards	Amount
Totals:		
Heart and vascular diseses	176	30,399
Lung diseases	84	6,661
Blood diseases and resources	81	5,976
Total	341	43,036

THE 1974 PROGRAM LEVELS

Mr. Flood. Finally, take a look at page 75 of your justifications. You have another table there. Adjust that table so that, first, you include the 1973 appropriation obligated in 1974 and, second show the true program levels where this multiple-year funding business is proposed.

You can do that for the record.

Dr. Cooper. Yes, sir.

[The information follows:]

National Heart and Lung Institute

Obligations by Budget Activity
Showing "True" Program Levels
in 1974 - 1975
(Amounts in thousands)

Budget Program	1973		1974		1975	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Heart and vascular diseases....................	---	$146,465	---	$188,577	---	$182,688
Lung diseases................................	---	28,345	---	42,679	---	47,228
Blood diseases and resources..................	---	41,672	---	50,635	---	50,626
Intramural laboratory and clinical research.....	358	19,267	345	21,632	345	22,445
Research management and program services........	287	12,110	318	15,586	318	16,988
Total obligations.........................	645	247,859	663	319,109	663	319,975

National Heart and Lung Institute

Obligations by Budget Mechanism
Showing "True" Program Levels
in 1974 - 1975
(Amounts in thousands)

	1972		1973		1974		1975	
	No.	Amount	No.	Amount	No.	Amount	No.	Amount
Grants								
Regular								
Non-competing	975	$81,140	983	$96,473	996	$111,538	1,195	$131,177
Competing	220	16,434	182	17,470	172	16,205	200	11,778
New	262	22,989	210	15,536	400	22,954	411	27,614
Supplemental	(138)	2,856	(199)	3,309	(150)	3,366	(125)	2,500
Subtotal	1,457	123,419	1,375	132,788	1,568	154,063	1,806	173,069
Special								
Heart cooperative drug study	56	3,514	55	4,495	54	4,900	1	1,000
Research career programs	178	5,040	179	4,925	233	6,590	170	5,000
Subtotal	234	8,554	234	9,420	287	11,490	171	6,000
Total Grants	1,691	131,973	1,609	142,208	1,855	165,553	1,977	179,069
Fellowships								
Non-competing	28	249	43	401	32	316	417	5,985
Competing	11	85	1	20	0	0	0	0
New	105	977	28	381	408	5,594	260	5,000
Supplemental	0	0	0	0	0	0	0	0
Subtotal	144	1,311	72	802	440	5,910	677	10,985
Training Grants								
Non-competing	307	14,330	178	11,282	150	8,718	60	5,360
Competing	31	2,842	36	2,507	10	140	0	0
New	19	1,263	6	279	15	200	0	0
Supplemental	(8)	121	(6)	276	0	0	0	0
Subtotal	357	18,554	220	14,344	175	9,058	60	5,360
Intramural Laboratory & Clinical Research		18,259		19,267		21,632		22,445
Research & Development Contracts		44,599		59,128		101,370		85,128
Research Management & Program Services		9,552		12,110		15,586		16,988
TOTAL		224,248		247,859		319,109		319,975

COOLEY'S ANEMIA

Mr. Flood. Just a year ago, exactly a year ago, the National Institutes of Health told the committee that "A request for proposal" for a contract to develop an effective and inexpensive test on Cooley's anemia was being prepared and that the National Heart and Lung Institute would award such a contract early in fiscal year 1974.

Well, now the committee has just received another special report on Cooley's anemia from the National Institutes of Health saying that this contract is now supposed to be awarded early in fiscal year 1975.

What kind of hanky-panky is this now? Are you going to keep changing this date every year just hoping we will forget about it or Cooley's anemia will go away or what?

Dr. Cooper. I wish Cooley's anemia would go away but not for that reason. To examine the question of screening, the National Institutes of Health Inter-Institute Coordinating Committee on Cooley's Anemia, of which Dr. French Anderson of the National Heart and Lung Institute is chairman, sponsored in April 1973, an international workshop in which this question of developing an effective and inexpensive test was examined. This panel concluded that a mass screening program should not now be undertaken, but that a small pilot program should be carried out and evaluated in order to determine if a mass screening program would be beneficial from a sociological point of view. Representatives of the Cooley's Anemia Foundation, which had previously been a strong spokesman for the development of a mass screening technique, were present at the workshop and agreed with this conclusion. The workshop also concluded that the present screening techniques are perfectly adequate for a pilot screening program. Even though the National Heart and Lung Institute is not responsible for implementation of the screening portion of the National Cooley's Anemia Control Act, we have agreed to carry out this pilot screening program because of the importance of the knowledge that would be obtained. I would be happy, Mr. Chairman, to provide the program summary of the workshop which pertains to screening and a list of its participants.

[The information follows:]

COOLEY'S ANEMIA WORKSHOP—SUMMARY OF PROGRAM

(April 10–11, 1973)

DETECTION AND DIAGNOSIS APPROACH: SCREENING

Presentation

Screening is, in itself, an area requiring research. In prospective screening (finding individuals at risk in a population) evidence is needed to determine if mating patterns are truly affected by people acquiring personal genetic knowledge. Furthermore, it is essential to learn what psychological effects such knowledge might have on the counselee. It would be inappropriate for this workshop to recommend studies in screening if, in fact, screening itself is detrimental.

Discussion

While there was considerable uncertainty at first as to whether or not the group's first responsibility (in view of the wording in the legislation) was to make a recommendation on the best methods of screening, general agreement was eventually reached that it was important that this advisory group state what it felt was the best course of action. It was decided that the main thrust of his aspect of the program should be to determine the effectiveness of genetic counseling as an adjunct with screening. The group felt that pilot programs in selected population groups should get first consideration for support. It is important in the programs to identify what is being measured, to evaluate the degree of the patient's understanding, to define the actual effect on mating decisions, and so forth. The approach used undoubtedly would vary between studies. It was discussed but not decided whether or not the approach used for counseling in other genetic diseases should be duplicated. The need for demographic studies on size of population at risk and frequency of the various thalassemia syndromes was pointed out (it was recognized that pilot screening programs might give misleading information since these would be going on in selected groups).

Specific points from discussion: (1) Dr. Rudolph Jackson, Chief, Sickle Cell Anemia Branch, National Heart and Lung Institute, pointed out the pitfalls in the Sickle Cell Anemia screening program. He advised that their experience should be taken into account before launching screening programs for Cooley's enemia. The group concurred. (2) Mrs. Anne Freedman, Executive Secretary of the Cooley's Anemia Foundation, described their preliminary screening efforts. These experiences emphasized the need for voluntary participation, preparation of the community, and confidentiality of the results.

Recommendations

(1) Pilot programs for evaluation of screening and counseling should take place before any large scale screening program should be undertaken. Information must be developed with regard to the impact of such programs on individuals and populations from a sociological point of view. Small scale, carefully controlled, pilot programs should be undertaken. Development and evaluation of screening methods for testing large numbers of individuals was considered not to be a high-priority goal. Present techniques seem compatible with the type of pilot screening programs proposed.

COOLEY'S ANEMIA WORKSHOP—LIST OF PARTICIPANTS

Name and institution

W. French Anderson, M.D.,[1] National Health and Lung Institute, National Institutes of Health, Bethesda, Md.
John Baiardi, Ph. D., New York Ocean Science Laboratory, Montauk, N.Y.
Arthur Bank, M.D., Columbia University, New York, N.Y.
Robin Bannerman, M.D., University of Buffalo. New York.
Samuel Charache, M.D., John Hopkins, Baltimore, Md.
J. B. Clegg, Ph. D., University of Liverpool, England.
Francesco Conconi, M. D., University of Ferrara, Italy.
Phaedron Fessas, M.D., University of Athens, Greece.
Bernard Forget, M.D., Children's Hospital, Boston, Mass.
Ann Freedman, Cooley's Anemia Foundation, New Hyde Park, N.Y.
Titus Huisman, Ph. D., Medical College of Georgia, Augusta, Ga.

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[1] Chairman.

Rudolph Jackson, M.D., National Health and Lung Institute, National Institutes of Health, Bethesda, Md.
Yuet W. Kan, M.D., University of California, San Francisco, Calif.
Ronald W. Lamont-Havers, M.D., NIAMDD, National Institutes of Health, Bethesda, Md.
Andrew Lang, M.D., Addenbrook's Hospital, Cambridge, England.
Paul A. Marks, M.D.,[1] Columbia University, New York, N.Y.
Bernadette Modell, M.D., University College Hospital, London, England.
David G. Nathan, M.D., Children's Hospital, Boston, Mass.
Arthur Nienhuis, M.D., National Health and Lung Institute, National Institutes of Health, Bethesda, Md.
Richard T. O'Brien, M.D., Yale University, New Haven, Conn.
Howard Pearson, M.D., Yale University, New Haven, Conn.
Sergio Piomelli, M.D., New York University, New York, N.Y.
Nevio Quattrin, M.D., Centro Sociale per lo Studio delle Emoglobinopatie Genotipiche di Napoli, Naples, Italy
Helen M. Ranney, M.D., University of California Medical School, San Diego, Calif.
Ronald Rieder, M.D., SUNY Downstate, Brooklyn, N.Y.
Richard Rifkind, M.D., Columbia University, New York, N.Y.
Peter Rowley, M.D., University of Rochester, N.Y.
Walter Schroeder, M.D., Medical College of Georgia, Augusta, Ga.
Elias Schwartz, M.D., Children's Hospital, Philadelphia, Pa.
George Stamatoyannopolos, M.D., University of Washington, Seattle, Wash.
David Weatherall, University of Liverpool, England
Maxwell Wintrobe, M.D., University of Utah, Salt Lake City
Edward Zaino, M.D.,[1] Mercy Hospital, Rockville Centre, N.Y.
Merilyn C. Hiller (recorder), NIAMDD–EP, National Institutes of Health, Bethesda, Md.

Mr. FLOOD. This national plan required by the law, by your authorization legislation, was submitted to the Congress last July. What did that plan include for future research on the disease of this Cooley's Anemia?

Dr. COOPER. It appears in the line in that budget on the page in volume 1 under projections under sickle cell and other related blood diseases and it reflects a modest expansion from $16 million in fiscal year 1974 up to about a $20 million level by 5 years later.

It reflects again an appreciation that it is one thing to make research on the disease in question but not promise that we can really deliver a massive program of application before the questions are solved.

But we do think that there is a reasonable base of scientific effort that is going on in an inter-Institute fashion that will allow modest increase in that effort.

HEW SCREENING PROGRAMS FOR COOLEY'S ANEMIA

Mr. FLOOD. Again for the record list all the programs now throughout all of HEW that are actually screening or should be screening people, especially children, for this Cooley's anemia, and also how much was spent in fiscal year 1973——

Dr. COOPER. On screening?

Mr. FLOOD. Yes; and your estimate for 1974 and estimate for 1975, and don't forget your friend medicaid when you do that.

Dr. COOPER. Yes; I was going to mention that the screening effort in that response will require we get information from other agencies in the Department.

[The information follows:]

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[1] Chairman.

SCREENING EFFORT IN COOLEY'S ANEMIA

In 1973 and 1974 the Department, while conducting research programs in Cooley's anemia, has not supported screening programs. In response to a previous question it was reported that the NIH did convene in 1973 an international workshop in which the question of developing an effective and inexpensive screening test was examined. It was concluded that a mass screening program was not appropriate at this time, but that a small pilot program should be carried out and evaluated in order to determine if a mass screening program would be beneficial. While the NHLI is not responsible for implementation of the screening portion of the National Cooley's Anemia Control Act, it has agreed to consider starting a pilot screening program which is projected to cost an estimated $100,000 in its first year.

Mr. FLOOD. Mr. Robinson.

Mr. ROBINSON. Thank you, Mr. Chairman.

HEART DISEASE

Dr. Cooper, you mentioned that we still rank second in the incidence of heart disease in the world with only Finland coming ahead of us.

To what extent have you been able to identify the similarities that exist between these two countries that rank highest in this incidence that causes heart disease to be so much more a problem here than in other countries?

Dr. COOPER. These are two vastly different cultures.

Mr. ROBINSON. They are indeed.

Dr COOPER And, therefore, the identification of common factors is a very interesting comparison.

The level of physical activity is different. Although we haven't got really accurate data on their dietary patterns, we presume that in part their dietary patterns are different, although we think that certain aspects of their dietary consumption models, say, for example, the consumption of fat as a percentage of diet, are somewhat similar.

We do not know some of the ancillary factors about other environmental influences like hardness and softness of the water. We have not the information on the incidence of the other risk factors like high blood pressure or cigarette smoking, although the information we have would indicate that Finland, as well as most other countries on which we have any data at all, is in a similar pattern.

In other words, 15 percent or so of the population has high blood pressure. So that although they are extremely different culture and have some strikingly different facets, like exercise, climate, other environmental exposure, there are some things very much in common.

Perhaps the dietary pattern of fats, carbohydrates, and protein, high blood pressure, cigarette consumption, is very high. What role genetics has in this or the hereditary pattern is something which we are not really very familiar with. It is a long-winded way of saying I really don't know.

Mr. ROBINSON. But there are certain similarities?

Dr. COOPER. There are certain similarities.

Mr. ROBINSON. And that assists you in your research?

Dr. COOPER. Yes.

Mr. ROBINSON. Do you feel that you are researching those areas that offer the promise that the similarity would suggest? Are all of these being looked into or are some of them where you have simply not been able to explore the similarity?

Dr. COOPER. I think in some areas we are able to explore the similarities and we are testing it. In some areas I think the big gap area is that when the risk factor hypothesis was developed, the classical data—indeed it is a milestone for the world in the study of coronary artery disease—was the Framingham study here in the United States in the environs of Boston in 1948, lasted 20 years, and we are still analyzing that data.

The problem was that maybe we didn't measure all the right things. Maybe there are other risk factors that we have not yet identified. So I think that is also a flag for us, the need to look at other things that might be in common in the different cultures. So again I think there are some leads in that type of geographical pathology that gave us leads into other research but one of the more important ones is that maybe we have missed the boat in looking for some of the key issues.

EMERGENCY CARE FOR CORONARY VICTIMS

Mr. ROBINSON. Doctor, it is very apparent I think to all of us that there have been tremendous strides in the ability to provide emergency care for coronary victims over the period of the last few years. I know that in the hospitals in Virginia many of them that had no coronary care units 5 years ago now have them.

To what extent do you feel that a serious problem still exists with regard to being able to take care of these people that we do get to the hospital? Is there still a serious gap, in our ability to accomplish this?

Dr. COOPER. There is a serious gap but I am less concerned that the gap is in the provision of special coronary care units in the hospital because I think either in special units or in special monitoring systems in the hospital great progress, as you have mentioned, has been made. I think the great gap is in shortening the time from bringing the patient to the hospital or the care to the patient immediately after the onset of symptoms of chest pains.

We have done studies in which we are able to identify that people, indeed doctors, who have heart attacks, and doctors are some of the worst offenders, procrastinate. They get the chest pain and they say, "Oh, it can't be happening to me. It is indigestion. It is the flu. It is pleurisy," and they procrastinate and the average procrastination in the studies that we made ranges between 6 and 7 hours.

During that period of time the 6 and 7 hours is the steepest part of the curve. Vulnerability to sudden death is greatest in that period of time.

Now, it is a fact that over half the deaths that occur in acute heart attacks in this country each year occur before the patient receives any medical attention. If we could get them all to the modern hospital that has a coronary care unit or the principals of it then I think we could even make better strides. So that is the vulnerable period that we have to work on, shortening that gap of time.

Mr. ROBINSON. Doctor, are there certain cities or hospitals in the country that serve as models in terms of their ability to provide this kind of care as compared to others that you refer to as being superior?

Dr. COOPER. Yes. There are a variety of cities and hospitals that indeed you have supported through another agency in the Department in development of total emergency care systems, through the Health Services Administration, I believe, at the present time.

The importance of that is that it is the one thing to have the idea and the understanding but you have to have the total capacity of the community to respond. Jacksonville, Fla., is one of those and it has a very enhanced ability to respond, well organized system of getting the public aware of what to do, the response capability very rapid, the city hospital situation and ambulance system organized to get them to the right place in the shortest period of time.

Nashville, Tenn., is another one at a smaller level that has a very good organization of that kind. There are more and more cities that are seeking that type of development.

STROKE

Mr. Robinson. With regard to stroke, Doctor, has any attempt been made to evaluate the factor of mental tension with respect to the incidence of stroke? Is it possible to do so?

Dr. Cooper. I don't know the answer to that one, mental tension related to stroke. I could answer it in mental tension related to heart disease in which a great deal of interest has recently been generated on the concept of stress.

Personality, anxiety in the relationship of the type of individual that is more prone to get a heart attack. Since the people who have heart attacks are more prone percentagewise to have strokes I presume that there are data, but I just don't know that right off the top of my head.

EARMARKING OF FUNDS

Mr. Robinson. Doctor, you mention in your statement that the formula requiring that 15 percent be spent on lung and 15 percent on blood diseases "must be carefully monitored."

What do you mean by "carefully monitored"?

Dr. Cooper. What I mean by that, Mr. Robinson, is that if the budget rises and the allocation for the area is made on a formula basis, we have to make sure that the scientific opportunities are commensurate with the moneys available.

The determination of 15 percent at a smaller budget area in which there is sort of an oversupply or abundance of new ideas of things that need to be done is no problem.

But say you had a budget of $500 million next year, and 15 percent of that is $75 million, and we went from an expenditure of $40 million to $75 million in one jump. I would have to be very careful in trying to justify that that is in the best interest of the total program.

That is what I mean by that. So I think that a formula of itself is not a solution to the problem and is not a substitute for a careful evaluation and judgment.

LIPID RESEARCH CLINICS

Mr. Robinson. You mention that there are 12 Lipid Research Clinics Are they generally distributed geographically so that they are available to the public on a basis that is considered reasonable?

Dr. Cooper. Yes. We attempted to include that factor because what we were trying to accomplish in that program as one of its main initial objectives is to determine the prevalence of the lipid patterns in this country.

The basic information that had been gathered was drawn from the Framingham population in Boston, a population of a community in Tecumseh in Michigan, a community around Albany and Baltimore.

What we wanted to do was to see if the conclusions that had been drawn from that about what is a normal cholesterol, how many people have it or have normal triglycerides, was a reflection of what happened nationwide, so it was important that we have some distributed around the country.

So that was a factor in the determination for that network.

Mr. ROBINSON. Do each of these clinics handle approximately the same number of people?

Dr. COOPER. Yes, sir. It is approximately the same number of patients. However, the geographical catchment areas have to be somewhat different because of the density of population.

Mr. ROBINSON. I would like to call your attention to some figures on pages 58 and 60 of your justifications and see if it is either that I don't understand it or they are inconsistent.

At the bottom of page 58 under "Decreases" under "b." you list "competing completed or converted to noncompeting" and you have a figure of $42,525,000.

Then on page 60 also under the "b." explanation of decreases, you say:

"The amount of $42,525,000 reflects the completion or conversions of 611 competing grants in 1974 to a competing status in 1975."

Mr. REEDER. This would be "Noncompeting status."

Mr. ROBINSON. I thought it was inconsistent and I just wanted to be sure.

UNITED STATES-U.S.S.R. COOPERATIVE STUDY

Finally, Doctor, I would like to ask about the implementation of the United States-U.S.S.R. cooperative study, the status of it and the process by which these medical and surgical techniques are compared.

Dr. COOPER. The United States-U.S.S.R. program in cardiovascular disease currently is comprised of six tasks with one under study for future consideration.

The six tasks are, first, a comparison of the biochemical characteristics of the populations of this country with those of the Soviet Union in key cities, for populations at risk of arteriosclerosis.

In other words, it would be the mirror image of our research clinical network being compared with clinics being set up in Leningrad and Moscow, in particular that first stage. They have agreed to use the same technology, our same protocols, the same input characteristics for data management as we have, the same evaluations of their cardiovascular status for comparison. All that has been accomplished. We expect to be getting some comparative data within the very near future. The basic work of standardizing techniques, translating manuals, training technicians to our way of running our lipid clinic network has been accepted by them and we expect to be monitoring their data through our coordinating center here in North Carolina, as a matter of fact.

The second task is aimed at comparing the treatment of coronary artery disease, different modes of treatment. It so happens in the Soviet Union that the surgical treatment of coronary artery disease by what is called the coronary bypass operation is done on a very small scale.

Their cardiologists do not let their surgeons operate on their patients although it is my perception that the surgeon would be pleased to do it.

In this country, as you are probably well aware, coronary artery bypass surgery is done very frequently, probably 25,000 or so cases a year in this country. This gives us an opportunity to compare patients, to compare those treated surgically and nonsurgically. It becomes very difficult in our own population to convince either the patient or the doctor that we should be able to randomize them and have one subjected to surgery and one not to surgery.

By happenstance eventually we are able then to compare a population that we can characterize by the same criteria in the two different countries if we can pull it off.

This again is in the stage now of agreement on development of the protocol. It is essential here to make sure we are reading the same disease as the same disease because the comparison of the result of treatment depends on that. That is the second task.

The third task is a basic more fundamental joint effort at studying metabolism of the heart. As I mentioned in my statement, some of the more exciting basic work going on in cardiology at the present time is the recognition that by changing the metabolic capability of the heart, particularly at times of injury or occlusion of the vessels, one can limit the area of injury that is induced. This had been come upon independently in the Soviet Union as well as by scientists in our country.

They have sort of a different chemical approach than our chemical approach and this effort could permit a great deal of perhaps unnecessary duplication in this country when we can view their data on a comparative basis.

The fourth area is an area which is directed toward the problem of congenital heart disease. They have a clinic over there in which their primary interest at the present time is in the surgical diagnosis and treatment of the infant under 1 year of age that has congenital defects of the heart and how to approach the diagnosis and treatment of these patients.

We, in my opinion, are considerably advanced over the Soviet Union in this area and in this area we have a great deal to offer them about our experience in large numbers of patients that have been diagnosed and treated by a wide variety of different surgical approaches and diagnostic efforts and have good followup techniques.

The Institute is currently completing a natural history study of congenital heart disease, one of 6 cooperative studies that was set up about 8 years ago. We have a considerable running start on this, and they will be the beneficiaries of that particular cooperative area.

The fifth area relates to the problem of sudden death, the problem you were talking about before. Now the Soviet Union says they have a very well standardized world-talked-about system of emergency care in Moscow and particularly in the major cities.

This gives access to test in a well-controlled population in which the city is divided up into quadrants with a very rapid call system for emergency care, whether the detection of that kind of patient will make any difference on the death rate from coronary artery disease. That has just begun this year.

We are comparing the populations at this point in time to see indeed whether they have the same interpretation of the incidence that we have. It is only this year that we are beginning to get data in the cardiovascular field, whereas in the cancer field for many years working through the International Cancer Union they have much more data on the incdence, the epidemiology of the cancer, in the Soviet Union than we have on cardiovascular disease.

That is why it is always qualified when I say Finland. I don't really know what the data are in the Soviet Union.

The sixth one is on blood transfusion, particularly as it is used in massive transfusion related to cardiac surgery, and we are particularly interested in their incidence of hepatitis, the safety of the blood, their methods of preservation, and yield of fractions from the blood.

That is also just new.

Under consideration is the final task which is not agreed upon as yet. These are techniques on mechanical replacement or total replacement of the heart, mechanical hearts, artificial hearts, are of great interest to them. It is another area where we have considerable technological advantage. We are exploring what types of programs to do with them in the future. We are currently expending perhaps $500,000 to $550,000 by the end of this year on the American portion of that comparative effort.

FEDERALLY SUPPORTED HEART AND LUNG RESEARCH IN VIRGINIA

Mr. ROBINSON. And lastly, Doctor, I wonder if you would list for the record the extent to which heart and lung research is being federally supported in my home State of Virginia.

Dr. COOPER. We will be pleased to do so.

Mr. ROBINSON. Thank you.

Dr. COOPER. I have it here. If you want to wait a minute I will tell you right now.

Mr. ROBINSON. If you will, just put it in the record.

[The information follows:]

NATIONAL HEART AND LUNG INSTITUTE

SUPPORT OF HEART AND LUNG RESEARCH IN THE STATE OF VIRGINIA, GRANTS AND CONTRACTS, FISCAL YEAR 1973

	Research grants	Training grants	Fellowships	Contracts	Total
Control Systems, Inc., Arlington				$311,200	$311,200
Hazelton Laboratories, Vienna				207,788	207,788
JRB Associates, Inc., Arlington				1,030,050	1,030,050
Max Folty Farms, Luray				78,000	78,000
Medical College of Virginia, VCU, Richmond	$1,475,710	$103,086	$28,822		1,607,618
Meloy Laboratories, Inc., Springfield				64,911	64,911
USPHS Hospital, Norfolk	12,313				12,313
University of Virginia, Charlottesville	785,404	138,914	122,283		1,046,601
Total, Virginia	2,273,427	242,000	151,105	1,691,949	4,358,481

Mr. FLOOD. Mr. Patten.

Mr. PATTEN. Dr. Cooper, it is good to see you again because you got a good start in life, born in New Jersey.

ADEQUACY OF BUDGET

Would you say generally your budget is not as controversial as, say, some of the others? Do you think you are getting by pretty easily with your work?

Dr. COOPER. I wouldn't say the budget isn't controversial but I believe as Disraeli did, sir, that the health of the people is the determination of the strength of the Nation. I think it is for that reason basically that the programs are less controversial in that sense.

Mr. Patten. The truth is we don't have the pressure on us concerning your appropriation that we have on some other subjects. That might be because it is funded fully. Yet you are not on the front page as you were, say, when Dr. DeBakey was here and we had heart transplants. I haven't heard you mention that. I thought if I lived 5 years I wouldn't die of heart trouble.

HEART TRANSPLANTS

What happened to all our headlines about heart transplants? Has it subsided?

Dr. Cooper. Yes, it has subsided substantially. Heart transplants are still being done, being done at about the rate of one or two a month, but they are being done largely for investigative therapy.

There was a considerable decrease in the enthusiasm of potential patients after they realized what the initial results of the procedure were and there was also a decrease in the amount of potential donors after the public discussion took place.

But I think the more important aspect is that the physicians themselves and the cardiologists and surgeons recognized that some of the preliminary considerations which seemed initially to make heart transplantation very practical proved scientifically not to be so.

For example, the heart muscle as a big massive muscle, it was thought maybe it wasn't antigenic, maybe it wouldn't reject, but it has long since been learned now that this is not the case, so that the activity that is going on in this realm is very good and we are supporting that work but it is largely of an investigative nature, even in patients, and it is very little in the news these days.

SCREENING OF SCHOOLCHILDREN

Mr. Patten. You had a lot to say about genetics and hereditary environment. I would like to get a quick reaction to how much of a look do we take at 54 million of our young people who are in the public school system.

I think it is about 54 million. I well know what my physical was back in 1912.

Dr. Cooper. I think the level of attention being paid to that is steadily improving. I think what you are pointing to is for many years it was a matter of looking at your teeth and giving you an eye test.

Mr. Patten. You need not even take your shoes off.

Dr. Cooper. That is right, but I think as a reflection of what the awareness has been, for example, in Georgia there has been a very effective program going on now in the elementary schools in which the children are being introduced to the concept if you can take care of your teeth you can take care of your heart, and they are learning about what blood pressure is and how it is taken and the children are having their blood pressure taken in schools and some of these other tests in school population.

In Des Moines, Iowa, in populations in Louisiana, this is improving steadily.

HEART FUND

Mr. Patten. In that connection we are faced with emotion and pathos with a drive to raise money for the heart fund. I know it is out of your line. Remember Walter Winchell used to be a great one on the Damon Runyon Heart Fund. Do you have a little personal observation about how the public meets these demands? Do you think the money is well spent?

Dr. Cooper. I will speak for the heart field. I think it is well spent. I think it is an excellent complementary activity to the Federal effort. I think they can do things, and do do things we cannot do and that need to be done.

By creatively working with the volunteer agencies we can avoid creating Federal networks for the distribution of several vital pieces of information. In other words, I feel that the Institute needs on certain occasions to utilize the heart associations for distribution of important information as we are doing right now in high blood pressure.

Also, they do constructively support community programs and local investigators that are brand new in areas that we do not test because they are not yet tried or advanced to the level at which we can.

I think this is a good complement to the Federal effort and should be maintained.

SMOKING AND HEALTH

Mr. Patten. This cigar is about the only habit I have which isn't fattening or immoral. You keep saying cigarettes. I am glad you don't include cigars. To listen to you, a lot of my habits are upside down.

Dr. Cooper. I think we do overdo it.

Mr. Patten. I tell my wife that, and she won't listen to me.

Dr. Cooper. I think it is a matter of degree. I think prudence is the marker, and I think as a matter of life we have to adjust.

I in no sense would advocate a rigid exclusion or prohibition of any of these things that you like. I think it is a matter of degree.

Mr. Patten. When you look at people, and bearing in mind the remarks you have made—and all of your profession talking in a similar vein—how much do you think 200 million people listen to you or respond to you? For instance, my doctor says to me if you take off 40 pounds, I think you will function better.

Are you ever discouraged when you see—like the Government says, smoking for 57 reasons is no good, it hurts your hemorrhoids, it hurts your eyes, and so forth. What is there about us as individuals that we just don't pick up and pay attention to what is said to us?

Dr. Cooper. I think it is a question, in my own personal opinion as an instant expert, everybody wants to know what is in it for me.

In certain programs when you can motivate the public, it is because you have a message to tell them what will be good for them. When you try to convince somebody to give up something that is enjoyable but they are not sick, that is a very difficult motivation process to accomplish.

On the other hand, when we do it, say, in high blood pressure—and let me do some advertising here with Jimmy the Greek—the problem is that it is a disease. It is not a question of whether you like it or not. The problem is you don't feel it at that point in time, and it is our ability to convince you that you have high blood pressure even though you don't feel bad. As a consequence, we have a leg up on the motivation process. That is a totally different ball game.

I think the question then is one largely of motivation, and it is something we have to learn how to do better in translating the fruits of research into practical application in the prevention of chronic disease.

EFFECTS OF CLIMATE ON CORONARY DISEASE

Mr. PATTEN. Rockefeller would leave New Jersey and go down to Florida as he got older and gave the dimes away down there. You are saying Finland has the highest incidence. In listening to undertakers, they tell me wait until you see the cold weather, we will be busy. Can you put your finger on cold air or exposure as bad for circulatory problems, and it is better to be a sun worshiper if you get older?

Dr. COOPER. I think it is. I think we could demonstrate for you a seasonal variation, particularly in the Northeast, Northwest, and central part of the country.

Mr. PATTEN. Undertakers will tell you when the cold weather comes in February, they bury more people.

Dr. COOPER. The adjusted death rate in the Southwest is less for heart disease than in the Northeast. Strangely enough, not in the Southeast, but for different reasons.

Mr. PATTEN. Thank you, Mr. Chairman.

NEW, PRACTICAL MATERIALS FOR MEASURING AMOUNT OF INJURY TO HEART MUSCLE

Mr. MICHEL. Dr. Cooper, you refer in your statement to "new, practical methods" that have been devised to locate and measure the area or amount of injury to the heart muscle that follows a heart attack. What are these methods?

Dr. COOPER. The best or most promising technique for measuring the amount of injured heart muscle associated with a heart attack takes advantage of an enzyme which is released from heart muscle when it becomes damaged. Several measurements for the amount of this enzyme in the blood must be done sequentially, and from this one can calculate an estimated amount of heart muscle that has been damaged. In another technique, the electrical signals from the heart are characterized as they appear at several dozen different locations on the chest surface; from the pattern of abnormality the site and extent of injury or infarction involving the front and side surfaces of the heart can be mapped. This technique offers its greatest promise for measuring the effects of treatment which is expected to reduce the amount of heart muscle undergoing damage. Other very exciting developments utilize radioisotopes, some of which go into areas of injury, others of which go only into normal tissue. Perhaps in the more distant future we will also have techniques in which the character of ultrasound reflection can be utilized for detecting injured heart muscle.

SERUM LIPIDS

Mr. MICHEL. On page 3 of your statement, you mentioned studies relating to the lowering of serum lipids. Is this all part of one study, or are they different? How long do you anticipate the study period to run? How long will it be before you will have some results?

Dr. COOPER. There are two different recently initiated studies relating to serum lipid lowering. The lipid research clinics' type II coronary primary prevention trial and the multiple risk factor intervention trial. These studies will be described in detail in a report on clinical trials to be prepared for inclusion in this testimony as requested by the chairman. The former, initiated in July 1973, is anticipated to run for 7 years after a 2-year recruitment phase; the latter from 1972 to 1981. The duration of these studies is based on projections of the length of observation needed to observe significant treatment effects. Findings will be periodically scrutinized throughout the period of these trials for significant effect.

Mr. MICHEL. For the record, would you amplify on the new method for measuring serum lipids? Where is it available, how is it done, what will it cost the patient, and who should take it?

Dr. COOPER. The new method for measuring serum lipids was developed in our specialized center of research on arteriosclerosis in New York City. It is a semiautomated technique that takes advantage of the turbidity produced in human serum when specific polyanions and polycations interact with the lipid-carrying proteins in the blood. It appears to allow a quick, low-cost diagnosis of elevated lipids (cholesterol and/or triglyceride) in the blood. The method is now being experimentally evaluated and compared to older assay procedures in ongoing clinical trials. If its consistent accuracy and precision can be demonstrated after widescale clinical evaluation, it will be available for use by all of this country's clinical laboratories.

ARTIFICIAL HEART PROGRAM

Mr. MICHEL. What progress has been made in the artificial heart program? Where are you with respect to implantation? What is your budget for this program, compared with last year and the year before? What special problems are you having the most difficulty overcoming?

Dr. COOPER. Better pumps have been developed, and pump linings now have less problems of blood clotting. The efficiency of thermal energy sources has been increased. Energy sources utilizing electricity have made major strides. There has been considerable further experience with bench testing and testing of the devices in animals.

It is hoped that a circulatory assist device suitable for clinical investigative use for periods up to 2 weeks will be available within 12 to 18 months. This is not a replacement for the heart, but a pumping device which shares or completely takes over the burden of the main pumping chamber of the heart, the left ventricle.

The budget for the total artificial heart program, including the blood-compatible materials and the artificial lung and oxygenator projects decreased from $10.2 million in 1972 to $9.9 million in 1973, but is increasing to about $10.3 million in 1974. The segment devoted strictly to artificial heart and circulatory assist devices has grown slightly over these same 3 years and will be approximately $8,250,000 in fiscal year 1974. All contracts for 1974 have not been let as of this time.

The special problems which are most difficult to overcome for the most immediate clinical application, the short term circulatory assist device, are the pump lining, which is still not free of clot formation problems, and the logistics of adequate animal tests to assess and prove the safety of the device for clinical use. For those devices which will have long term use measured in years, there are additional problems of durability of certain mechanical components and the need for long term energy sources or for the transmission of energy into the body reliably and without complications.

Mr. MICHEL. In your statement on page 5 you say that much of the technology and "know how" developed in the artificial heart program has been useful in developing and improving respirators or artificial lungs. In what ways has this been so?

Dr. COOPER. Techniques developed in the artificial heart program have been utilized in improved artificial lungs which are now undergoing evaluation. Other developments have led to an improved and more compact respirator which has undergone extensive testing; it has been taken up by the private sector as a commercial device.

PREVENTION AND TREATMENT OF RESPIRATORY DISTRESS

Mr. MICHEL. You refer to "entering a new era of research on the lung," and say your approach to the prevention and treatment of respiratory distress syndromes, bronchitis, emphysema and pulmonary vascular disease will be "revolutionized." What do you mean by this? "Revolutionized" is a pretty strong word, isn't it?

Dr. COOPER. While "revolutionized" is indeed a strong word, it is not inapporpriate in this context because in the past the major reseach emphasis has been on measures of pulmonary function. This provided us with information about what had happened but not why the changes occurred. The new approaches that depend on biochemistry and immunology will lead us to the causes of lung diseases and hence open the way to preventing these disorders and to curing them when they occur.

Mr. MICHEL. You mention, on page 6, blood testing to identify individuals who lack certain enzymes and are thus prone to lung disorder. Have you gone so far as to pin down a direct relationship between the lack of certain enzymes and specific lung problems? What do you do with a blood test, then? Counsel the patient to change his job or his climate, if necessary? Anything beyond that?

Dr. COOPER. It has been demonstrated that a relationship exists between the risk of developing emphysema and the absence of an enzyme (alpha-1-antitrypsin) in individuals who inherit this deficiency from both parents (are homozygous for the deficiency). It remains to be proven whether individuals who inherit the deficiency from only one parent (are heterozygous) are also at risk. In view of the high risk for the homozygous deficiency, such individuals profit from counseling to avoid chest colds, smoking, or residing in areas where environmental pollutants are abundant. Moreover, the fact that we know of a specific enzyme that is involved in the development of one type of emphysema is providing us with an experimental tool to study the causes of this disorder and to look for other genetic factors that may be involved. This is an important step to preventing emphysema.

SICKLE CELL DISEASE

Mr. MICHEL. What is the current extent of your sickle cell effort?

Dr. COOPER. The current effort in sickle cell addresses the disorder from two general standpoints. First there is the area of research and development, including basic and clinical research, clinical trials of therapy, and clinical application. In this area, investigation is in progress to better understand the sickling mechanism in sickle cell disease, the basis and treatment for the complications manifested; development and trials of agents which will alter the sickling phenomenon; and the improvement of means of diagnosing the presence of sickle hemoglobin.

Second, there are demonstration activities in education, testing, counseling, and rehabilitation. In this area, various methodologies in sickle cell education, testing, counseling and rehabilitation are being evaluated with the aim of making those methodologies felt to be of significant value available to the ongoing health care delivery system and general community for use as indicated. Generally accepted educational approaches are presently being carried out to better inform and educate the public about sickle cell disease and sickle cell trait. This includes the dissemination of information to health providers, educators, other professionals and lay, as well as "target" groups.

Mr. MICHEL. What is your budget compared with last year?

Dr. COOPER. Funding for research in sickle cell disease and related diseases totaled $14.5 million in 1973 for grants and contracts supported by this Institute. The estimated level of funding for this year is $15.5 million.

Mr. MICHEL. You say that urea does not appear to be effective. Does anything else look promising?

Dr. COOPER. At present time, the agent sodium cyanate appears to have promise in reducing the frequency of crises in sickle cell anemia. Active investigation of this agent is in progress, including studies of toxicity and side effects. Depending upon the findings of these studies, a clinical trial will be carried out to test the efficacy of this agent. Several other agents are also under investigation and include carbamyl phosphate, alkylating agents, trace elements, and various amino acids.

ALLOCATION OF RESOURCES FOR LUNG AND BLOOD DISEASE PROBLEMS

Mr. MICHEL. You say that "In compliance with Public Law 92-423, 15 percent of our resources for research are being directed to lung problems and over 15 percent to blood disease problems," and that this has resulted in a change of emphasis within the Institute's program. Change of emphasis in what ways? Is this budgetary pattern quite different from the past? Doesn't this rather rigid earmarking put you under some constraint? What kinds of problems could be created by this?

Dr. COOPER. The shift in emphasis has been to develop and expand, more rapidly, our attack on lung and blood diseases. The emphasis has been to make them major programs responsive to basic research opportunities and clinical studies that have been neglected in the past. The thrust of this emphasis is to establish the framework for achieving the needed fundamental studies and clinical investigations and trials that are necessary to assure a balance of program effort in both the lung and blood disease areas. The limits have provided a base for initiating and responding to new opportunities in each of these major disease areas. It has, by its very nature, required some aspects of the more developed field of heart and vascular diseases to stay in abeyance.

This type of budgeting is new and quite different from previous budgetary patterns. The earmarking of the specific funds has not put us under major constraints because of the need to establish a framework for taking advantage of the research opportunities in the various lung and blood areas. In this initial phase of formulation, the earmarking has given added impetus and has not posed difficulty within the overall current funding level. However, if these fixed percentages were applied to dollar commitments essential for implementation and application of research results in the more developed phases of the Institute's program, it would pose difficulties. This results from differences in resource needs for investigative purposes as opposed to developmental and applicational phases. The potential problems of fixing resource commitments through this means would, in effect, have major influence on the ability to respond to basic and applied research opportunities in the various disease areas; the capacity to implement needed activities under a broad national program for these diseases, including timely achievement of targeted program goals; and the needed flexibility for operation and translation of select medical research results in medical practice.

COOLEY'S ANEMIA

Mr. Conte. Will the planned National Research and Demonstration Center in Blood Diseases give any special attention to Cooley's anemia?

Dr. Cooper. We hope that the scope of work covered in the national research and demonstration centers concerning blood research programs will include work on Cooley's anemia. The specific work scopes of the program have not been determined since the proposals are under review at the present time.

Mr. Conte. You refer to the need for a simple screening process for Cooley's anemia. Will you describe the progress you are making on it?

Dr. Cooper. The subject of the need for an inexpensive screening test was discussed in great depth at the "Research Workshop in Cooley's Anemia" which was held in New York City in April 1973 by the National Institutes of Health Inter-Institute Coordinating Committee on Cooley's Anemia. At that time the problems arising from the screening and counseling programs of sickle cell anemia were emerging and, because of the similarity between sickle cell anemia and Cooley's anemia, it seemed wise that the lessons learned from the sickle cell screening programs should be applied to that of Cooley's anemia. Consequently, the workshop participants recommended, and the National Institutes of Health Inter-Institute Coordinating Committee on Cooley's Anemia agreed, to postpone development of a mass screening technique until the sociological effects and advisability of a mass screening program were determined by means of carefully controlled, small-scale pilot screening and counseling programs, and until such time when a more accurate, simple, inexpensive screening methodology could be developed. Presently available screening techniques may be adequate for such small-scale programs. While such pilot programs in screening and counseling were not the primary responsibility of the National Institutes of Health, when it became evident that such programs were not being initiated by other agencies, the National Institutes of Health, and specifically the National Heart and Lung Institute, began considering the development of plans for implementing such a program. Since it was too late to consider this in the National Heart and Lung Institute research plans for 1974, the program has been submitted in the National Heart and Lung Institute forward plan for 1975, for consideration within the priorities for the Institute's total research program.

Mr. Conte. Is any special group, or groups, of investigators doing unusually promising work toward developing such a process?

Dr. Cooper. Several groups, including Dr. Howard Pearson at Yale, are attempting to develop screening techniques which could be used on a large scale. To date, however, a simple, reliable, inexpensive screening procedure, which could be used for a mass screening program, has not been developed.

Mr. Conte. How many new projects directly on Cooley's anemia were funded in fiscal year 1973? Fiscal year 1974?

Dr. Cooper. I shall be happy to supply that for the record.

[The information follows:]

New projects in Cooley's anemia—fiscal year 1973

Short title and principal investigator:	*Amount*
Molecular Pathology of Genetic Disorders; Yoshida, Akira Y., D. Sc	$209, 440
Structure and Properties of Six Hemoglobins; Masur, Abraham, Ph. D	45, 230
Molecular Adaptation: The Hemoglobin System; Bonaventura, Joseph, Ph. D	79, 204
Subtotal	333, 874
In addition, the following grants competed successfully for renewal:	
Raman, Spectra of Heme Proteins and Related Molecules; Spiro, Thomas G., Ph. D	56, 136
Peptide Bond Formation and Hemoglobin Synthesis; Heintz, Roger L., Ph. D	41, 327
Total	431, 337

No new projects have been awarded to date for research in Cooley's anemia in 1974.

Mr. Flood. Thank you very much. gentlemen.

Dr. Cooper. Thank you very much.

JUSTIFICATION OF THE BUDGET ESTIMATES

NATIONAL INSTITUTES OF HEALTH

NATIONAL HEART AND LUNG INSTITUTE

Amounts Available for Obligation [1]

	1974 Revised	1975
Appropriation	$302,915,000	$309,299,000
Amount withheld (PL 93-192)	-13,365,000	.
Subtotal, adjusted appropriation	289,550,000	309,299,000
Real transfers to:		
"Health Services Planning and Development" (Emergency medical services activities)	-3,000,000	
"Departmental management" (For Department-wide reductions in public affairs)	-85,000	
Comparative transfers to:		
"Office of the Assistant Secretary for Health" (Transfer of administrative support activities to the Office of the Assistant Secretary for Health)	-77,000	
"Departmental management" (Transfer of accounting functions from the OS Working Capital Fund)	-9,000	
Comparative transfer from:		
"Departmental management" (Transfer of indirect cost negotiation function to the OS Working Capital Fund)	12,000	
"National Institute of General Medical Sciences" (Decentralization of scientific evaluation grants program)	358,000	
Subtotal, budget authority (base obligations)	286,749,000	309,299,000
Unobligated balance, restored	44,103,000	
Comparative transfer of restored unobligated balance to Research Resources for General Research Support Grants	-1,067,000	
Total, obligations	329,785,000	309,299,000

[1] Excludes the following amounts for reimbursable activities carried out by this account: 1974 $10,000; 1975 $10,000.

Summary of Changes

1974 Estimated obligations..................................	$329,785,000
1975 Estimated obligations..................................	309,299,000
Net change..................................	-20,486,000

	Base		Change from Base	
	Positions	Amount	Positions	Amount
Increases:				
A. Built-in:				
1. Within grade pay increases...	---	---	---	$223,000
2. Annualization of 1974 pay raise costs in 1975........	---	---	---	150,000
3. Federal Telecommunications System (FTS) rate increases	---	---	---	50,000
4. Bureau of Employee Compensation (BEC) rate increase...	---	---	---	10,000
5. Postage rate increase........	---	---	---	36,000
6. Extra day of pay.............	---	---	---	33,000
7. Building rentals and miscellaneous operating costs......................	---	---	---	265,000
8. Payment to NIH Management Fund......................	---	---	---	$1,154,000
Subtotal..................	---	---	---	1,921,000
B. Program:				
1. Research grants:				
a. Noncompeting continuations..........	---	111,538,000	---	38,300,000
b. Competing (new continuations & supplementals).	---	---	---	41,892,000
2. Fellowships..................	---	6,210,000	---	4,869,000
3. Research and development contracts..................	---	106,970,000	---	4,455,000
4. Intramural laboratory and clinical research..........	345	12,954,000	---	92,000
5. Research management and program services...........	318	12,624,000	---	202,000
Subtotal..................	---	---	---	89,810,000
Total, increases................	---	---	---	91,731,000
Decreases:				
A. Program:				
1. Research grants:				
a. Noncompeting completed or converted to competing status................	---	---	---	20,077,000
b. Competing completed or converted to noncompeting.............	---	---	---	42,525,000
c. 1974 obligations used to fund 1975 continuations	---	---	---	1,416,000
d. Special programs.........	---	11,490,000	---	5,490,000

	Base		Change from Base	
	Positions	Amount	Positions	Amount
Decreases: (Cont.)				
2. Training grants.............	---	$12,418,000	---	$10,418,000
3. Fellowships.................	---	6,210,000	---	394,000
4. Research and development contracts................	---	106,970,000	---	31,897,000
Total, decreases...............	---	---	---	112,217,000
Total, net change..................	---	---	---	-20,486,000

Explanation of Changes

Increases:

A. Built-in: The increases will provide: 1. $223,000 for withing grade pay increases in 1975; 2. $150,000 for the annualization of 1974 pay raise costs in 1975; 3. $50,000 for increases in Federal Telecommunications System (FTS) rates; 4. $10,000 for increases in Bureau of Employee Compensation (BEC) rates; 5. $36,000 for postage rate increases; 6. $33,000 for one extra day of pay in 1975; 7. $265,000 for increased building rental costs and other miscellaneous costs (including service and supply costs); and 8. $1,154,000 for increased costs of the NIH Management Fund for centrally furnished services.

B. Program:

1. Research grants:
   a. The amount of $38,300,000 in non-competing continuations represents the 400 new and 172 competing grants made in 1974 which will become non-competing in 1975.

   b. The amount of $41,892,000 in competing research grants reflects: 1) $27,614,000 for 411 new awards; 2) $11,778,000 for 200 competing continuations; and 3) $2,500,000 in supplementals.

2. Fellowships: The increase of $4,869,000 will provide for the newly established research training fellowship program. Approximately 260 new awards will be made in this program in 1975, bringing to a total of 660 the number of fellows receiving support.

3. Research and development contracts: The increase of $4,455,000 will provide for moderate increases in the renewal of contracts which support research in established programs in heart and vascular, lung, and blood diseases and blood resources.

4. Intramural laboratory and clinical research: The program increase of $92,000 will provide improvements in facilities relating to molecular hematology, pulmonary disease, and veterinary medicine.

5. Research management and program services: The program increase of $202,000 will provide for costs related to an expanded education and control program, particularly in high blood pressure.

Decreases:

A. Program:

1. Research grants:
    - a. The amount of $20,077,000 in non-competing continuations represents 225 non-competing regular research grants that were completed in 1974 or that are being converted to competing status in 1975.
    - b. The amount of $42,525,000 reflects the completion or conversion of 611 competing grants in 1974 to a competing status in 1975.
    - c. The decrease of $1,416,000 reflects the reduced funding required in 1975 due to multi-year funding of projects in 1974.
    - d. The decrease of $5,490,000 in Special programs represents 53 grants completed in the Heart Cooperative Drug Study and the multi-year funding of Research Career program awards in 1974.
2. Training grants: The decrease of $10,418,000 in 1975 is a result of multi-year funding of projects and the completion of 50 non-competing projects in 1974.
3. Fellowships: The decrease of $394,000 in 1975 is a result of multi-year funding awards and the completion of 22 fellowships in 1974.
4. Research and development contracts: The decrease of $31,897,000 in 1975 is a result of the multi-funding of several contract programs in 1974, including the Clinical Trials.

Obligations by Activity

Page Ref.		1974 Base *		1975 Estimate		Increase or Decrease	
		Pos.	Amount	Pos.	Amount	Pos.	Amount
76	Heart and vascular diseases	---	$166,649,000 (197,048,000)	---	$174,217,000	---	+$7,568,000
97	Lung diseases....	---	37,906,000 (44,567,000)	---	45,340,000	---	+7,434,000
106	Blood diseases and resources....	---	44,976,000 (50,952,000)	---	50,309,000	---	+5,333,000
114	Intramural laboratory and clinical research	345	21,632,000	345	22,445,000	---	+813,000
115	Research management and program services.........	318	15,586,000	318	16,988,000	---	+1,402,000
	Total obligations (bases)........	663	286,749,000	663	309,299,000	---	+22,550,000
	Total obligations		(329,785,000)				

Explanation of Changes (by activity)

A) Heart and vascular diseases. The increase of $7,568,000 will provide additional support to the several grant and contract programs in this area. Included are three clinical trials now in progress. These trials are the multiple risk factor intervention trial, the clinical trial on the lipid hypothesis, and the hypertension detection and follow-up program. Specialized centers of research and individual-investigator research grants will also be increased, particularly in the areas of ischemic heart disease and hypertension. New research and demonstration will be established.

B) Lung diseases. The increase of $7,434,000 will allow additional support for research in pediatric pulmonary diseases and in emphysema and chronic bronchitis, particularly through an expansion of the specialized centers of research network and by the establishment of pulmonary research and demonstration centers. There will also be additional pulmonary young investigator awards.

C) Blood diseases and resources. The increase of $5,333,000 will supplement existing specialized research centers and allow the establishment of one or two research and demonstration centers. Increases in contract programs will provide research support in thrombosis and in blood resources to expand hepatitis and transplantation biology programs. There will also be additional programs in prevention, education, and control.

D. Intramural laboratory and clinical research. The increase of $813,000 includes $721,000 for mandatory "built-in" changes and $92,000 for development of molecular hematology, pulmonary, and veterinary laboratory facilities.

E. Research management and program services. The increase of $1,402,000 includes $1,200,000 for mandatory "built-in" changes and $202,000 for expanded education and control programs, particularly in high blood pressure and for increased support of the Interagency Technical Committee.

Obligations by Object

	1974 Estimate	1975 Estimate	Increase or Decrease
Total number of permenent positions.....	663	663	---
Full-time equivalent of all other positions............................	51	51	---
Average number of all employees.........	696	696	---
Personnel compensation:			
Permanent positions..................	$10,497,000	$11,348,000	+$851,000
Positions other than permanent........	702,000	733,000	+31,000
Other personnel compensation..........	320,000	331,000	+11,000
Subtotal, personnel compensation....	11,519,000	12,412,000	+893,000
Personnel benefits.....................	1,532,000	1,621,000	+89,000
Travel and transportation of persons....	784,000	750,000	-34,000
Transportation of things................	160,000	160,000	---
Rent, communications, and utilities.....	825,000	1,161,000	+336,000
Printing and reproduction..............	300,000	300,000	---
Other services:			
Project contracts.....................	106,970,000	79,528,000	-27,442,000
NIH Management Fund..................	11,331,000	12,485,000	+1,154,000
Other................................	6,167,000	5,905,000	-262,000
Supplies and materials..................	3,141,000	3,180,000	+39,000
Equipment..............................	1,459,000	1,459,000	---
Grants, subsidies, and contributions....	185,597,000	190,338,000	+4,741,000
Total, obligations by object..........	329,785,000	309,299,000	-20,486,000
Total obligations excluding 1973 appropriation......................	286,749,000		

Significant Items in House and Senate Appropriations Committee Reports

Item	
1974 House Report	
1. The Committee felt that the increased emphasis on lung diseases is nevertheless constrained by a lack of trained and knowledgeable personnel. The Committee recommended that the Institute address the immediate and future pulmonary manpower needs. (Page 31)	1. The Lung Division is establishing the Pulmonary Young Investigator Award. Initial awards will be made in 1974 with significant program expansion scheduled in 1975. These awards are made to individual investigators to support research projects which have been self-initiated. In addition, the Pulmonary Academic Award program will be virtually doubled in 1974 and 1975 over the 1973 level of funding.
2. The Committee noted that their past recommendations for increases in positions have not been effected. (Pages 31 and 32)	2. In 1974 an additional 51 positions was allocated to the Institute. These positions will be carried forward in 1975. The position level represents the maximum allowable within currently available resources. By optimum utilization of the positions assigned to it, the NHLI has been able to make considerable progress on new initiatives, including the mandates of the National Heart, Blood Vessel, Lung, and Blood Act of 1972, while continuing to maintain excellence in the Institute's Intramural Laboratory and Clinical Research program.
1974 Senate Report	
1. The Committee provided $23 million for high blood pressure screening programs of detection, follow-up evaluation, and appropriate treatment. (Page 43)	1. The Hypertension Detection and Follow-up Program is now in its operational phase. This randomized study is measuring the extent to which a systematic hypertension management program can reduce coronary morbidity and mortality. Patients in the program, who were screened from a larger population, are now in the treatment stage in a five year program to determine the effectiveness of anti-hypertensive therapy. In addition, an extensive high blood pressure education program is being implemented to educate the public and physicians in the importance of case-finding in hypertension, appropriate treatment of hypertensive patients, and maintenance of treatment.

1974 Senate Report (Continued)

2. The Committee emphasized the need for more trained physicians in the pulmonary specialty. (Pages 43 and 44)	2. See item (1) in the House Report (above)
3. Committee mandate that sufficient amounts of good quality blood be available to all. (Page 44)	3. Work continues on the problem of identifying hepatitis carriers and removing the hepatitis virus from blood. Study of the consequences of cytomegalovirus transmission by blood and chemical contaminants leached from blood bags is progressing.

Authorizing Legislation

Legislation	1975 Authorized	1975 Appropriation requested
Public Health Service Act Title III, Part A, Section 301--Research and Investigation, In General	Indefinite	$309,299,000
Title IV, Part B--National Heart and Lung Insitute: Section 414	$45,000,000	
Section 419B	475,000,000	
Title XI, Genetic Blood Disorders	53,700,000	

National Heart and Lung Institute

Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
1965	118,125,000	117,006,000	116,763,000	117,078,000
1966	133,235,000	138,035,000	135,285,000	133,429,000
1967	139,147,000	145,827,000	155,827,000	155,827,000
1968	157,846,000	157,846,000	165,255,000	157,817,000
1969	160,310,000	154,695,000	162,695,000	157,502,500
1970	151,088,000	151,088,000	171,526,000	161,831,500
1971	164,923,000	169,207,000	194,207,000	186,798,000
1972	188,225,000	203,299,000	243,299,000	224,302,000
1973*	247,075,000	290,784,000	340,784,000	290,784,000*
1974	265,000,000	281,415,000	320,000,000	300,014,000**
1975	309,299,000			

* Note: This appropriation authority was the continuing resolution. The appropriation amount was the House Allowance, which was the lower of the House or Senate amounts in the first vetoed bill.

** Appropriation after reduction, $286,749,000

Justification

National Heart and Lung Institute

Authorizing Legislation: Public Health Service Act: Title III, Part A, Section 301, Research and Investigation, in General; Title IV, Part B--National Heart and Lung Institute, and Title XI, Genetic Blood Disorders.

	1974 Base		1975 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits...........	663	$13,051,000	663	$14,033,000		+$982,000
Other expenses...........	---	273,698,000	---	295,266,000		+21,568,000
Total..................	663	286,749,000	663	309,299,000		+22,550,000

General Statement

The most comprehensive review of the programs of the National Heart and Lung Institute in the history of the Institute was completed in 1973. This review was accomplished by almost 250 medical and scientific advisors who composed 28 separate task groups within four panels established for heart and blood vessel diseases, lung diseases, blood diseases, and blood resources. The Institute's assessment of this review has resulted in a progressive National Program based on the national health problem with reference both to accomplishments and to goals.

A conceptual strategy for the National Program Plan was presented nearly one year ago in the National Heart and Lung Institute Summary (National Heart, Blood Vessel, Lung and Blood Program, Volume I, May 1, 1973, submitted to the Congress July 24,1973). In this initial program strategy three underlying principles were outlined:

- The long-range goal must be to improve the health of the American people.
- Programs for achieving this goal must be based on an orderly progression of sequenced activities from acquisition of fundamental knowledge to the application of existing knowledge.
- Evaluation of the use of knowledge--both before its application in health care delivery and after to determine its impact on the health of the American people--will be the key to meeting national health goals.

The Problem

The maturation of many research-proven ideas, methods and technologies, viewed in relation to the increasing health problems of heart, blood vessel, lung and blood diseases, indicates that the next few years could bring significant new discoveries and health benefits for the American people. Great strides have been made in prevention, both real and potential, in diagnosis and in medical and surgical treatment of these major diseases. The result brings new hope for patients suffering from them. In fact, death rates from some of these diseases have levelled off or even decreased in the last few years.

At the present time, the diseases addressed by the National Program together cause more than one million deaths each year in the United States. In their chronic forms, they affect more than 30 million Americans. The loss of productivity through disability alone is enormous.

Diseases of the heart and blood vessels are by far the largest problem. They account for more than half of the annual deaths from all causes in the United States, thus making this country's rate among the highest of the developed nations. Although the toll is heaviest in the older ages, a quarter of the deaths occur under age 65.

- Coronary heart disease, which includes heart attack, causes 675,000 deaths each year, many of which occur suddenly and unexpectedly; four million persons in this country have had a heart attack or suffer from angina pectoris.

- Every year 200,000 individuals die as the result of a stroke; 1.7 million persons are at least partially incapacitated from having suffered a stroke.

- Hypertension, which predisposes to stroke and heart failure, affects 23 million Americans, 13 million under age 65.

If heart and blood vessel diseases could be eliminated as causes of death, the gain in life expectancy would approach 11 years, more than four times the gain that would be achieved by the elimination of any other cause of death.

The chronic lung diseases are also a serious health problem.

- Emphysema, chronic bronchitis and asthma afflict 14 million individuals, more than 11 million of them younger than age 65.

- Each year, emphysema, pneumonia and hyaline membrane disease kill 100,000 Americans.

Thrombosis and diseases of the blood are responsible for much acute and chronic disease.

- Venous thrombosis and pulmonary embolism hospitalize 300,000 persons annually.

- Sickle cell anemia and severe hemophilia afflict 50,000 to 75,000 persons.

- Post-transfusion hepatitis is estimated to occur annually in 20,000 to 30,000 patients and to be fatal in about 3,000.

The impact of the heart, blood vessel, lung and blood diseases on the nation's economy is great. Each year, health expenditures for these diseases are more than $9 billion, and the value of present and potential earnings lost because of the illness and death they cause amounts to more than an additional $30 billion.

Accomplishments/Goals

The immediate goal of the National Heart and Lung Institute is to secure the additional knowledge and techniques needed for early diagnosis, and effective treatment of existing disorders of the heart, blood vessels, lungs and blood and to demonstrate their application to the health care problems of the country. The long-range goal is prevention and elimination of disease. It is important to state clearly the lessons that have been learned about scientific discoveries necessary to solve the great problems of these diseases.

First, although we have learned much about the heart and blood vessels, lungs and blood, our areas of ignorance are still far greater than areas of complete understanding. The following are but a few examples:

- In the past three decades, we have learned how to prevent rheumatic fever and rheumatic heart disease by treating the antecedent streptococcal infection with penicillin. For those patients who developed rheumatic heart disease before that time, we have learned how to repair or replace badly damaged heart valves. But we still do not know how to ensure that every child with a sore throat has a throat culture or how to treat all susceptible children long enough to prevent heart disease.

- In the past three decades, we have learned how to use new drugs to lower blood pressure in hypertensive patients to lessen the risk of strokes and heart failure. But we still do not know what causes most forms of high blood pressure, how to motivate the population to be screened for high blood pressure, or how to initiate and maintain effective therapy in all those with high blood pressure.

- We have learned how to catheterize the hearts of small babies to identify congenital heart lesions, and how to correct them by open heart operations. But we do not know how many congenital cardiac defects are genetic or how many reflect the environment of the fetus, and, except for some defects known to be due to rubella virus, we do not know how to prevent congenital heart disease.

- We know how, by surgical procedures, to correct or by-pass atherosclerotic obstructions in the arteries. But we do not know how to prevent atherosclerosis or how to diagnose and treat it early.

- We have sophisticated physiological tests that tell us precisely the functional defects of diseases of lungs. But we do not know the cause of pulmonary emphysema, how to stop its progress even if detected early, or how to prevent heart disease caused by emphysema.

- We know the specific clotting factor whose deficiency causes hemorrhage in patients with hemophilia. But to treat these patients requires harvesting the factors from more than 50 percent of the national blood supply. We do not know how to obtain these factors with reasonable cost-effectiveness; neither have we discovered alternative treatments.

We tend to obscure our ignorance by making it seem that a problem has been solved when it has, in fact, been only half solved. We must face up to our ignorance in many matters and recognize that an entirely different type of knowledge than we now have will be necessary to fully solve these problems.

Second, by far the surest way to save the public's health dollar in the long run is to obtain a clear enough understanding of the mechanisms causing heart, blood vessel, lung or blood diseases to permit prevention or complete cure. The less we know about a disease, the less specific is the treatment and the greater the cost. Specific prevention and definitive treatment usually cost relatively little and are easily translated into effective action.

- Twenty-five years ago, all we could offer patients with tuberculosis was nonspecific sanatorium or surgical care which was very costly and not very effective. We now have specific chemotherapy; it is both effective and cheap.

- Finding factors that produce rheumatic fever and a way to prevent rheumatic heart disease have proved to be far less costly than modern diagnosis and surgical treatment of patients with damaged heart valves.

- It is far less expensive to provide rubella vaccine to future mothers before their child-bearing age than to perform heart surgery to correct the congenital heart defects that rubella causes.

In the long run, investment in fundamental and clinical research to learn the mechanisms and causes of diseases and to prevent them has been far less expensive than paying for half-way measures, the results of which can only be a reduction in disability.

Third, to bring the best possible health care to the people of our country and, ultimately, to prevent disease, we must accelerate two campaigns: (1) to apply what we now know as effectively as we can, and (2) to gain new knowledge and new understanding of the basic biological processes and mechanisms underlying normal heart, blood vessel, lung and blood functions; of the biochemical, genetic, nutritional, behavioral, social environmental and other processes that lead to diseases of these systems; and of ways to prevent or counteract these diseases.

Both campaigns are essential. We cannot tell patients who are ill with a disease that we are concerned only with the prevention of such disasters in others; for them, having the best available treatment may be a matter of life or death. We must not have all basic research and no applied; but neither must we have all applied research and no basic.

Fourth, contrary to popular conception, it can be documented that important new knowledge rarely comes through sudden "breakthroughs"; research goals are almost invariably reached by a steady accumulation of knowledge--bit by bit--until finally the last bit secures a major advance. In biological research, crash programs often crash!

Similarly, great clinical advances rarely burst upon the scene as the result of mission-oriented, commission-directed programs, but come at a logical time when a broad advance in basic biologic science (often not directed toward the prevention or treatment of a particular disease) has made the clinical discovery nearly inevitable. Mission-oriented programs can then accelerate the achievement of the final specific goal.

One of the most important and certainly the most dramatic advances of the past two decades has been the development of open heart surgery. To the lay public and to many physicians and scientists, open heart surgery stands out as a great achievement of mission-oriented, goal-directed research. Although the development (by mission-oriented research) of a pump-oxygenator was absolutely essential to open heart surgery, it is crucial to the understanding of scientific discovery to realize that its development was itself possible only because of many earlier discoveries that were not mission-oriented, such as:

- Discovery by a physiologist of heparin, a substance that prevents blood clotting;

- Discovery by an immunologist of blood groups that led to blood typing and safe blood transfusions (and today to safe blood use in pump oxygenators);

- Studies of red blood cells, their natural lifespan and how to preserve their life outside the body--which led to the storage of blood for emergencies and then to blood banks.

- Studies by biochemists on the diffusion and exchange of oxygen and carbon dioxide, essential for construction of artificial oxygenators.

But successful open heart surgery required more than a pump-oxygenator. It also required accumulation of considerable knowledge in many biologic fields. It had to await basic research on the heart's conducting system and on arrhythmias that led to devices to control serious arrhythmias; on fluid and electrolyte metabolism that permitted long surgical procedures; and on anesthesia, respiratory physiology and mechanics of ventilation that permitted proper ventilation and anesthesia of a patient with an open chest. Other important contributions were the discovery of the electrocardiograph, of hypothermia, of techniques for electively stopping and restarting the heart, and of chemotherapy and antibiotics.

Knowledge flows in both directions. Thus, the identification and study by surgeons of new problems in patients who have undergone open heart surgery stimulated renewed research efforts and produced new knowledge in basic research in many fields.

A recent analysis of 175 scientific discoveries that had to be made to permit the great clinical advances of the 1950's and 1960's in the treatment of heart, blood vessel, lung and blood diseases, showed that 36 percent were basic discoveries completely unrelated to these diseases; 31 percent were made in basic research designed to contribute to solution of a clinical problem; and 33 percent were made as a result of applied mission-oriented research. Therefore, an essential part of the Institute's philosophy is that both applied science (and development and engineering) and basic science are essential. The Institute hopes that it will be recognized that the last event leading to a dramatic clinical advance is possible only because of scores or hundreds of earlier discoveries. We should not talk in terms of supporting either basic or applied, or targeted or nontargeted research. We must support mission-oriented research to alleviate suffering and reduce disability and we must support nontargeted research to uncover knowledge not yet imagined by the most competent commissions, panels or task forces appointed by public or private agencies.

Fifth, the all important clue to the cause and prevention of atherosclerosis or emphysema, as well as many other diseases, may come from scientists working in an unrelated field.

- When Karl Landsteiner discovered human blood groups, he was investigating basic problems in immunology; he was not then aware he was making safe blood transfusion possible.

- When Roentgen discovered X-rays, he did not realize it would enable physicians to visualize the heart, lungs, and blood vessels of their patients.

- When Cournand and Richards passed a catheter into the heart of a man, it was not to develop methods of diagnosing congenital or acquired heart disease; they wanted to measure the oxygen in mixed venous blood to learn more about basic physiologic problems of pulmonary gas exchange.

- When Alexis Carrel developed the new science of suturing blood vessels and transplanting arteries, veins and whole organs, it was a necessary first step to his main goal to study basic life processes and\ the metabolic requirements of each organ for optimal function.

- When Davies and Brink devised an "electrode" to measure the oxygen used by nerve cells, they had no idea that it would become an essential monitoring device in every intensive care unit for measuring blood oxygen.

These examples make it clear that a successful effort against heart, blood vessel, lung and blood diseases will depend, in part, upon strong and sustained support of basic and mission-oriented research in other fields of science, as well as those fields directly concerned with these diseases.

DHEW - National Institutes of Health

CROSSWALK - 1974 COLUMN 1975 PRESIDENT'S BUDGET

INSTITUTE: National Heart and Lung Institute
(Dollars in thousands)

	Research Grants								
	Regular Program		Specials	Training Programs		Laboratory and Clinical	Research and Development	Other Direct	
Program	Non-competing	Competing	Other	Grants	Fellowships	Research	Contracts	Operations	Total
1974 Base Obligations									
1. Heart & Vascular Diseases........	$69,200	$25,600	$6,731	$6,060	$4,484		$54,574		$166,649
2. Lung Diseases....................	20,100	7,220	1,939	1,628	732		6,287		37,906
3. Blood Diseases & Resources.......	22,238	6,925	589	412	600		14,212		44,976
4. Intramural Laboratory & Clinical Research......................						$21,632			21,632
5. Research Management & Program Services......................								$15,586	15,586
Subtotal.....................	111,538	39,745	9,259	8,100	5,816	21,632	75,073	15,586	286,749
Unobligated Balance Restored									
1. Heart & Vascular Diseases........		2,900	1,730	3,152	317		22,300		30,399
2. Lung Diseases....................		648	225	950	38		4,800		6,661
3. Blood Diseases & Resources.......		648	276	216	39		4,797		5,976
Subtotal.....................		4,196	2,231	4,318	394		31,897		43,036
Total Obligations...............	111,538	43,941	11,490	12,418	6,210	21,632	106,970	15,586	329,785

DHEW - National Institutes of Health

CROSSWALK - 1975 COLUMN 1975 PRESIDENT''S BUDGET

INSTITUTE: National Heart and Lung Institute
(Dollars in thousands)

Program	Research Grants						Laboratory and Clinical Research	Research and Development Contracts	Other Direct Operations	Total
	Regular Program		Specials		Training Programs					
	Non-competing	Competing	GRSG	Other	Grants	Fellowships				
1. Heart & Vascular Diseases........	$77,900	$26,588		$3,170	$1,460	$8,075		$57,024		$174,217
2. Lung Diseases....................	26,900	7,518		2,270	440	1,410		6,802		45,340
3. Blood Diseases & Resources.......	24,961	7,786		560	100	1,200		15,702		50,309
4. Intramural Laboratory & Clinical Research......................							$22,445			22,445
5. Research Management & Program Services......................									$16,988	16,988
Total Obligations...............	129,761	41,892		6,000	2,000	10,685	22,445	79,528	16,988	309,299

National Heart and Lung Institute

Budget Mechanism

	1974 Estimate*		1975 Estimate	
	Number	Amount	Number	Amount
Grants				
Regular				
Non-competing................	996	$111,538,000	1,156	$129,761,000
Competing....................	156	15,422,000	200	11,778,000
New..........................	377	21,613,000	411	27,614,000
Supplemental.................	(131)	2,710,000	(125)	2,500,000
Subtotal.....................	1,529	151,283,000	1,767	171,653,000
Special				
Heart cooperative drug study.	54	4,900,000	1	1,000,000
Research career programs.....	144	4,359,000	170	5,000,000
Subtotal.....................	198	9,259,000	171	6,000,000
Total Grants.................	1,727	160,542,000	1,938	177,653,000
Fellowships				
Non-competing................	32	316	400	5,685,000
Competing....................	0	0	0	0
New..........................	380	5,500	260	5,000,000
Supplemental.................	0	0	0	0
Subtotal.....................	412	5,816	660	10,685,000
Training Grants				
Non-competing................	150	8,100,000	40	2,000,000
Competing....................	0	0	0	0
New..........................	0	0	0	0
Supplemental.................	0	0	0	0
Subtotal.....................	150	8,100,000	40	2,000,000
Intramural laboratory & clinical research......................		21,632,000		22,445,000
Research & development contracts.		75,073,000		79,528,000
Research management & program services.....................		15,586,000		16,988,000
TOTAL........................		286,749,000		309,299,000

* Excludes 1973 appropriation restorations.

Heart and Vascular Diseases

	1974 Base *		1975 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits...............	---	---	---	---	---	---
Other expenses...............	---	$166,649,000	---	$174,217,000	---	+$7,568,000
Total.............	---	166,649,000	---	174,217,000	---	+7,568,000
Subactivities:						
Arteriosclerosis...........	---	43,556,000	---	43,542,000	---	-14,000
Hypertension..............	---	30,322,000	---	31,922,000	---	+1,600,000
Stroke.....................	---	2,430,000	---	3,600,000	---	+1,170,000
Coronary Heart Disease.....	---	35,973,000	---	37,278,000	---	+1,305,000
Congenital & Rheumatic Heart Disease.............	---	7,334,000	---	7,600,000	---	+266,000
Peripheral Vascular Disease	---	3,381,000	---	3,504,000	---	+123,000
Cardiomyopathy & Infections of the Heart.............	---	3,427,000	---	3,551,000	---	+124,000
Arrhythmias................	---	11,456,000	---	11,871,000	---	+415,000
Cardiac Failure & Shock....	---	16,226,000	---	16,814,000	---	+588,000
Other Heart & Vascular Diseases.................	---	---	---	2,000,000 1/	---	+2,000,000 1/
Prevention, Education, & Control..................	---	2,000,000		3,000,000	---	+1,000,000
Research Manpower Development.............	---	10,544,000	---	9,535,000	---	-1,009,000
Total.................	---	166,649,000	---	174,217,000	---	+7,568,000
Budget Mechanism:						
Research Grants:						
Regular..................	---	94,800,000	---	104,488,000	---	+9,688,000
Special..................	---	6,731,000	---	3,170,000	---	-3,561,000
Subtotal..............	---	101,531,000	---	107,658,000	---	+6,127,000
Fellowships..............	---	4,484,000	---	8,075,000	---	+3,591,000
Training Grants.........	---	6,060,000	---	1,460,000	---	-4,600,000
Research & Development Contracts.............	---	54,574,000	---	57,024,000	---	+2,450,000
Total...............	---	166,649,000	---	174,217,000	---	+7,568,000

1/ Research and Demonstration Centers for multi-categorical heart disease research.

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* Excludes 1973 appropriation restorations.

Objectives, 1975

Based on a National Heart and Lung Institute budget of $309,229,000 it is anticipated that the Heart and Vascular Diseases budget will be approximately $174,217,000 for grants and contracts. This budget would provide an increase of $5,599,000 for the estimated level necessary to meet commitments for the non-competing continuation of regular research grants and for competing projects to insure a stable continuation of research grant programs. It would supplement the 20 established Specialized Centers of Research in arteriosclerosis and hypertension by $2,028,000 for a variety of programs, some of which are noted below. Of major importance in 1975 is the funding of National Research and Demonstration Centers for research in heart disease. These centers are envisioned as a national resource attached to a major medical complex dedicated to working in close collaboration with the Institute to further its goals through a multi-disciplined, coordinated, yet flexible approach to research, education, both public and professional, and demonstration of the applicability of the results of research. $2,000,000 is estimated in 1975 for the establishment of one to three centers. Fiscal increases as each center develops will run to approximately $3,000,000 each in the third year. Another important new program being developed in 1974 and 1975 concerns the education, prevention, and control of the cardiovascular diseases as presented in the Institute's National Program. Demonstration and control programs are essential mechanisms to bring about the transmission of medical research advances into general application for the benefit of the public. An additional $1,000,000 is requested for 1975 in both research grants and contracts. The clinical phase of the Heart Cooperative Drug Study is scheduled for completion in 1975. This budget includes $1,000,000 for continued statistical and programmatic evaluation for this study in 1975. There is a net decrease of $649,000 in training programs. This is comprised of a reduction of $4,600,000 in the phase-out of graduate cardiovascular training grant programs as presented to the Congress last year. Assistance to graduate students and post-graduates in the life and social sciences will be more equitably provided under the expanded general assistance programs available to all graduate students through the Office of Education. There are, however, certain identifiable research manpower needs relevant to particular areas or disciplines, fields, or specialties. To meet these needs the NIH is to implement a new fellowship program this year, which was announced by Secretary Weinberger on July 9, 1973, and which has excited wide interest in the biochemical research community. An increase in 1975 of $3,591,000 is requested to insure the supply of skilled manpower as an essential element in a national effort against the heart and vascular diseases. There have been identified research manpower needs in behavioral research, microcirculation, bioengineering, genetics, protein/immunochemistry, thrombo-atherogenesis, pediatric metabolism, and epidemiology/biostatistics. There is an increase of $2,016,000 for arteriosclerosis clinical trials discussed below.

Arteriosclerosis (Hardening of the Arteries)

Program goals

A large amount of knowledge has been developed about the cause and pathogenesis of arteriosclerosis. Significant positive statistical associations have been made between arteriosclerotic disease and high blood fats, hypertension, physical inactivity, heavy consumption of cigarettes, personality type, and other variables. It is not yet known how these variables are associated with arteriosclerosis. However, current research on molecular and tissue interactions has elicited information that promises to explain its development and offer opportunities for prevention.

Clearly, it would be better and less costly to prevent the formation of arteriosclerotic plaques than to attempt to treat the resultant vascular disease and its sequelae. There exist many leads to prevention and to a better understanding of arteriosclerosis. Some of these leads come from research on metabolism, normal and abnormal structure and function of the arteries, and genetic and environmental factors which influence atherogenesis. A priority need exists to define more completely the pathogenesis of atherosclerosis and to conduct controlled clinical trials. The Institute plans to continue research emphasis on pathogenetic mechanisms of arteriosclerosis and to evaluate preventive measures in clinical trials.

- The NHLI overall goal in arteriosclerosis is to obtain better understanding of its basic process and to improve the prevention, diagnosis, and treatment of the process and its sequelae.

Opportunities and needs

All aspects of the study of arteriosclerosis would be greatly advanced if there existed diagnostic instruments for detecting small changes in atherosclerotic plaques. The present state of technological development suggests that this is possible. Current approaches include highly sophisticated techniques such as ultrasonic methods, x-ray densitometry, and computer-assisted image enhancement of complex image signals. These techniques are not yet adequate, but indicate a feasible and promising technical area where rapid and successful progress can be expected.

Many needed studies of chronic arterial disease cannot be conducted in man. Suitable animal models of human disease would bring about many economies of time and effort in the attack against arteriosclerosis. Nonhuman primate models with chronic experimental arteriosclerosis and chronic experimental hypertension need to be developed. These animals would allow us to study the maintenance and regression of atherosclerotic plaques, local biochemical and cellular changes in advanced plaques, and treatment of advanced plaques. Animals with spontaneous metabolic disease such as elevated blood lipids of diabetes need to be bred to create colonies for research in these disorders related to arteriosclerosis.

Recent studies have shown genetic influence on the metabolism of lipoproteins on the excretion of sterols, and on the atherogenetic reaction of the arterial wall. This research, presently incomplete and in need of both confirmation and detailed investigation, will be fundamental to the identification of patients at high risk of arteriosclerosis and to the development of rational treatment.

Several clinical trials are currently underway to seek ways to prevent coronary heart disease. These efforts are aimed at determining the value of controlling the risk factors of high blood lipids, high blood pressure, and smoking. Potentially useful drugs are under study. Such trials of potential preventive measures have both theoretical and practical value. Controlled comparison of surgical versus medical management should be done to evaluate these forms of treatment.

Actions

To meet these needs and to take advantage of the opportunities in arteriosclerosis research, the Institute plans to:

- Emphasize pathogenetic studies within existing research programs, centers of research, and lipid research clinics.
- Stimulate the development of sensitive, specific, invasive and non-invasive, convenient and safe diagnostic techniques that can be used to determine arteriosclerotic changes in vessels.
- Evaluate current techniques for the diagnosis of hyperlipoproteinemia and other risk factors and encourage the development of better ones. Implement an intervention study in high risk subjects to test the effectiveness of lipid lowering by selected means to reduce cardiovascular mortality and morbidity.
- Establish colonies of suitable animal models with particular reference to nonhuman primates with arteriosclerotic or hypertensive disease for use in research on arteriosclerosis, hypertension, and cerebral vascular disease. Animal research will also be encouraged in genetics related to arteriosclerosis.
- Expand current population studies in the Institute's Lipid Research Clinics, Specialized Centers of Research in Arterio-

sclerosis, and clinical applications and prevention programs to include in-depth genetic studies.

- Encourage experts in psycho-sociology and behavioral research to study problems associated with health education and attitudes, motivation, and compliance as these relate to the prevention of arteriosclerosis, hypertension or stroke and to the therapy and rehabilitation of patients with these diseases.

- Conduct a Multiple Risk Factor Intervention Trial to determine whether, for men at above average risk of death from coronary heart disease (because of elevated serum cholesterol, elevated diastolic blood pressure, and cigarette smoking) a special intervention program will result in a significant reduction in mortality from coronary heart disease.

  In June, 1972, the Institute awarded contracts to establish 8 clinical centers and a coordinating center for planning and conducting this trial. An additional 7 centers were established in June, 1973, and the final five centers have been added in 1974. This study will entail a 6-year period of clinical management.

- Provide for acquisition, analysis and storage of data on the prevalence of different types of hyperlipoproteinemia, especially among young age groups, with special emphasis on their relationship to diet as well as the prevalence of atherosclerosis in the different types of hyperlipoproteinemia.

- Promote further clinical, laboratory, and epidemiologic studies of personal attributes and living habits such as nutrition, exercise, obesity, tobacco usage, biochemical and hormonal patterns, psychosocial stress and behavior in relation to the occurrence of arteriosclerosis, coronary heart disease, stroke, and hypertension with particular regard to the onset of arteriosclerosis in the younger ages and in women..

- Expand current population studies and develop new epidemiologic studies of the role of environmental factors such as trace substances, water hardness, climate, geography, and occasional exposures in the pathogenesis of arteriosclerosis.

- Implement the US-USSR cooperative study to define the prevalence of different types of hyperlipoproteinemia, their relationship, environmental factors, especially nutrition, as well as many broadly defined cardiovascular risk factors.

Recent Advances and progress

Basic research

The processes leading to the development of atherosclerosis are closely related to altered permeability of the walls of the arteries. Lipids are deposited in the wall more rapidly than they are removed. Experiments in living animals and isolated human blood vessels indicate that patterns of increased permeability which permit greater fat deposition are virtually identical to patterns of early atherosclerosis. The arterial wall is made more permeable by various hemodynamic factors such as constrictions, increased blood flow, and increased blood pressure, as well as by injury to the lining of the blood vessel.

Studies on the transport of lipids to and from the arterial wall have been extended by the development of better techniques of isotopically tagging lipid and protein components of plasma lipoproteins to permit analyses of the mechanism of transport of these molecules into the arterial wall, either as units or in parts. Methods of determining alterations in "chemical barrier" and wall ultrastructure have been developed. Examination of the transport of lipid molecules away from the arterial wall once they have been deposited indicates this to be a complex and slow process. The role of the vessel wall in atherogenesis is under investigation in some 70 major projects of which 10 are within Specialized Centers of Research.

The process of lipolysis (decomposition of fats) is central to the utilization of fats by the body, whether ingested in the diet or made in the tissues, and is a major determinant of blood lipid (fat) concentrations. The part played by various enzymes in the arterial wall during this process is being explored. The arterial wall contains enzymes capable of breaking down the lipids entering the wall from the blood. Lipoprotein lipase (a fat-splitting enzyme) has been the subject of intensive study almost continuously since its discovery at the NHLI 20 years ago. Scientists have now shown that there are at least two different lipases that can be liberated into blood to hasten lipid removal. One enzyme, coming from the liver, is believed to play a role in degrading lipid remnants, possibly for entry into the liver. The other acts primarily to degrade larger lipid particles, chylomicrons and very low density lipoproteins. Lipoprotein lipase is selectively absent in one human mutation (familial Type I hyperlipoproteinemia) leading to abnormal levels of lipid in the blood of these individuals. Other tissue enzymes capable of decomposing lipids have also been intensively studied this past year. New compounds have been found which may be involved in arteriosclerotic plaque formation. The previous observations on rapid and reversible effect of insulin on lipids have been further advanced and it is now possible to study more directly the nature of the effects of insulin and adrenal hormones in the handling of fats by the body.

Hyperlipidemia (high blood lipids or fats) is one of the major conditions associated with premature atherosclerosis, particularly coronary artery disease, and is one of the first rank problems facing American physicians, especially those engaged in preventive medicine. The NHLI has been a leader in promulgating new systems of classification and identification of causes and treatment of hyperlipidemia. The Institute's extramural Lipid Research Clinic Program had its birthplace within the NHLI Intramural Research Division. The prevalence of and mechanisms behind the human forms of hyperlipidemia are now being studied at the 12 extramural Lipid Research Clinics. The 12 clinics are collaborating on a protocol for central processing and evaluation of the heart, coronary, and major vessels of post-mortem examinations of Lipid Research Clinic patients. The central pooling and processing of all pathologic material in the Lipid Research Clinics' Central Pathology Laboratory at the NHLI will allow the gathering of useful clinical pathologic correlations regarding human hyperlipidemias.

There are currently approximately 160 major research projects concerned with fundamental and applied research on lipids as pathogenetic agents in atherogenesis and in metabolic disorders leading to arteriosclerosis. Approximately 60 of these are contained within the activities of the Specialized Centers and Lipid Research Clinics.

In several of the Institute's Specialized Centers of Research in Arteriosclerosis, improvements are now being made in invasive and noninvasive diagnostic methods for the recognition of atherosclerotic plaques in the blood vessels. Other fundamental studies involve the development and use of nonhuman primate models for studies on the development, progression, and regression of the atherosclerotic process.

Nutrition (basic and applied)

The Multiple Risk Factor Trial will have a strong nutritional component. The program objective of nutrition intervention is to reduce elevated serum cholesterol by adherence to a lipid-lowering diet. All men in the study will be taught to change their eating habits and food choices to obtain 30-35% calories from fat, less than 10% from saturated and approximately 10% from polyunsaturated fatty acids with the intake of cholesterol limited to 300 mg per day on the average. Weight control and correction of obesity will be undertaken when appropriate. Reduced intake of total carbohydrate and alcohol will be advised for men with elevated triglycerides, but only after the need for these restrictions is demonstrated by failure to respond adequately to the basic diet.

A common detailed nutritional questionnaire and 1 day diet recall has now been inserted into all 12 Lipid Research Clinic prevalence studies. Coding rules and centralized computerized data center have been created. This will allow the Lipid Research Clinics the opportunity to evaluate the role of diet both in the dyslipoproteinemias detected during their population surveys and its association with vascular disease incidence.

Nutritional factors in relation to lipid metabolism and atherogenesis are being investigated in approximately 30 projects, the majority within lipid clinics and specialized research centers.

Clinical research

The Lipid Research Clinics have agreed to an in-depth study of all the relatives of patients found to have primary hyperlipoproteinemia during their prevalence studies. They are also in the process of finalizing a collaborative cord blood protocol that promises to fully evaluate the utility of using placental cord blood for the provisional diagnosis of familial hyperlipoproteinemia.

In the Specialized Centers of Atherosclerosis where prevalence studies are a component, extension to in-depth genetic studies of index cases is also being encouraged. A Framingham offspring study is underway to provide a one-time characterization of the offspring of 1,644 spouse sets who were part of the original Framingham cohort. More than 2,200 offspring have already undergone evaluation. This study will permit the study of familial and genetic associations between parents and offspring in regard to cardiovascular risk factors, particularly the lipid and lipoprotein fractions. The NHLI Twin Study has now collected data on over 600 sets of identical twins aged 25-55 under a standard protocol. Preliminary results indicate major genetic determinants of the observed variability in height, weight, blood pressure and serum cholesterol. An offspring study of the subjects of the Honolulu cohort of the Honolulu-Hiroshima-San Francisco Heart Disease Study has begun.

The Coronary Drug Project, a secondary prevention clinical trial of lipid altering drugs has reached an average follow-up of 58 months on an enrolled population of 8,400 men aged 30-64, who have had one or more myocardial infarcts prior to entry into the study. The clinical phase of this trial, which has already uncovered unfavorable features of several drugs, is scheduled to terminate in 1975 and the decreased funding level is reflected in the budget tables.

A common problem potentially threatening all these trials is limited availability of adequate expertise to carry out multiclinic trials as well as a limited supply of acceptable study patients.

Clinical trial costs should plateau in 1975. Present programs related to the prevalence of lipid abnormalities and hypertension among children and young-to-middle aged adults are scheduled to be completed between 1976 and 1978. Programs will be continued or initiated in pathogenesis, instrumentation, epidemiology, genetics, nutrition, animal models, and behavioral studies.

Hypertension (High Blood Pressure)

Program goals

High blood pressure can be controlled and it is known that such control results in a reduced incidence of stroke and heart failure, and perhaps also reduced incidence of heart attacks.

The cause and pathogenesis of the most common form of hypertension is not understood and continuing research will be necessary to elucidate this. Because of the large numbers of people affected by hypertension, it would be especially desirable to be able to prevent it. Indeed, the National Heart and Lung Advisory Council has stated "The Council gives high priority to investigation of the causes of hypertension."

- The long-range goal in hypertension is to prevent it; the short-range goal is to optimize the utilization of effective treatment which currently exists.

Opportunities and needs

It is not known how beneficial treatment of mild forms of high blood pressure is. Since an estimated 19 million people have mild hypertension, it is important that this information be developed.

About four million people at any given time have hypertension of a degree known to be harmful. It can be controlled by medication with appropriate drugs. However, currently available drugs require close medical supervision and often have unpleasant side effects which make it difficult to use them for long periods of time in asymptomatic individuals. There is the need to develop improved pharmacologic agents without such side effects and without the need for meticulous, individually adjusted dosage.

Rational treatment and prevention of hypertension will require a thorough understanding of its causes and pathogenesis. While some current information about the formation and modulation of vasopressor polypeptides and related enzyme systems helps to explain pathogenetic mechanisms, little is known about its causes. An intensive examination of the etiology and pathogenesis of hypertension is essential.

Epidemiological data will be forth coming as a side product of the Hypertension Detection and Follow-up Program which began its clinical phase in February, 1973. Population data from 14 community clinical centers will become available to characterize prevalence of hypertension by a limited number of demographic, socioeconomic, and occupational characteristics. A total enrollment of 10,500 men and women between ages 30-69 have been enrolled to participate in this randomized study to measure the extent to which a systematic hypertension management program can reduce coronary morbidity and mortality.

An important component of the Hypertension Detection and Follow-up Program involves behavioral research as it relates to the identification of factors which enhance compliance to therapy or impede such compliance among individuals placed on anti-hypertensive drug management. Detailed characterization of participants is part of the baseline information obtained at the start of enrollment in the intervention program. This will allow comparison of noncompliers or poor compliers with those who are successful in following the prevention program.

Follow-up of the 5,000 participants in the Regular Care Group will provide general population data on the progression of high blood pressure and its manifest complications.

Data on high blood pressure from six prospective epidemiological studies in populations which have had follow-up observations and blood pressure measurements over 4 to 18 years are now available. Systematic analysis of these data to search for characteristics differentiating individuals who have hypertensive diseases are underway. Population data from the Puerto Rico, Honolulu Japanese American and Hiroshima Japanese American populations, Israel, and Yugoslavia are available to compare with the present 18 year follow-up data from Framingham.

Actions

To meet these needs and to take advantage of these opportunities, the Institute will:

- Emphasize research on the etiology and pathogenesis of hypertension, including its epidemiology, in many of the individual and specialized laboratories working on this problem.
- Conduct a Hypertension Detection and Follow-up Program to determine the effectiveness of a systematic approach using antihypertensive therapy in reducing mortality among those with elevated blood pressure in community-based populations.
- Implement clinical trials of antihypertension therapy in mild and labile hypertension.
- Evaluate new pharmacologic approaches to the treatment of hypertension utilizing existing research centers and pharmacologic expertise, with emphasis on new drug formulations.

Recent advances and progress

Approximately 220 grants are concerned with the multiple considerations that enter into research on the etiology and pathogenesis of hypertension. In addition there are some 20 projects including those in both the arteriosclerosis and hypertension centers that relate to the epidemiology of hypertension.

Specialized laboratories are continually working on various assays of angiotensins, aldosterone, and prostaglandins to determine more fully the role of each in the pathogenesis and etiology of hypertension. For the first time beginning this summer, clinical tests of an agent which blocks the conversion of Angiotensin I to Angiotensin II will be started. Since Angiotensin I is inactive on blood vessels while Angiotensin II is an effective constrictor, it will be possible to measure the effect on the blood pressure elevation when one effector is eliminated. If this test proves to be as useful as anticipated, more laboratories will be encouraged to use it in their studies. Three Hypertension Specialized Centers of Research have been selected to participate in this trial.

The regular research grant program is receiving and supporting an increasing number of projects on psychobiology (particularly stress) in the genesis of hypertension and will continue to develop a larger number of research programs in this area.

Varying combinations of available drugs are being tested for their effectiveness with respect to specific test results obtained on individual patients. It appears possible that specific therapy may soon be tailored to the functional aberations found in an individual hypertensive subject so that more effective therapy is achieved.

Stroke (Cerebrovascular Disease)

Program goals

The National Institute for Neurological Diseases and Stroke is primarily responsible for programs on those aspects of stroke that deal with brain injury and its consequences. The NHLI is responsible for programs on the cerebrovascular pathology that underlies the stroke. A liaison Joint Council Sub-committee exists for purposes of coordination and exchange of information.

- The goal of the NHLI program is to decrease the indicence of stroke through studies of the pathology and pathogenesis of cerebrovascular disease.

Opportunities and needs

To determine the etiology and prevention of stroke, animal studies of the effects of chronic arteriosclerosis and chronic hypertension on the arteries of the brain are needed. The goals of these animal studies will be to elucidate, by methods not applicable to man, the vascular pathology that leads to stroke.

Action

To deal with the cardiovascular problems which form the basis for cerebrovascular disease and stroke, the Institute will:

- Initiate studies in animals of the pathology of the lesions of chronic atherosclerosis and hypertension in the cerebrovascular arteries. Emphasis will be placed on those lesions that may contribute to ischemic stroke or arterial brain hemorrhage. Since little knowledge is available as yet about chronic changes in animal models, particularly in non-human primates appropriate for neurological examination, the chronic and special animal resources referred to in the sections on Arteriosclerosis and Hypertension can be utilized with minor expansion or redirection for the study of cerebrovascular disease.

- Continue prospective epidemiologic studies which are engaged in identifying environmental factors and personal attributes which predispose to increased risks of stroke. Maintain surveillance of stroke endpoints in the clinical trials discussed in the sections on Arteriosclerosis and Hypertension.

Recent advances and progress

There has existed for several years a liaison group between the National Institute of Neurological Diseases and Stroke and the National Heart and Lung Institute. The group has been drawn in part from the Advisory Councils of the two Institutes and in part by other appropriate experts and Institute staff. It has acted in information exchange, development of bibliographies, conferences and workshops and in similar activities.

Within the National Heart and Lung Institute there are currently only a small number of grants concerned with cerebral vasculature. The majority of these relate to man. There are only a few grants concerned with the effects of hypertension on vessels. These are in animals. They do not relate primarily to the cerebral vessels.

Coronary Heart Disease

Program goals

A research program focused on patients with acute heart attacks has developed information about pathophysiology; prognostic factors, pharmacological, surgical, and circulatory assist therapy; and techniques and instruments for conducting research in the acutely ill patient. These developments can now be built upon and more broadly used.

- A primary goal of the program is to develop improved therapy, rehabilitation, diagnosis, and improved understanding of the mechanisms resulting in symptomatic coronary disease.

Coronary artery bypass surgery has been developed in recent years to supplement medical management of coronary heart disease, particularly for the treatment of angina pectoris. This surgical technique uses a blood vessel graft to bypass a narrowed or occluded segment of a coronary artery. Over 25,000 such operations are now done annually with hospitalization costs in excess of $5,000 for each operation.

- A major goal is to establish the indications for and the effects of coronary artery surgery in the treatment of various forms of coronary heart disease.

Each year about 400,000 deaths from coronary heart disease occur before hospitalization, half of these occurring almost instantaneously or unwitnessed. Over three-quarters of these victims have known heart disease or high blood pressure before their sudden deaths, but in the rest sudden cardiac death is their first evidence of heart disease.

- Another major goal of the program is to develop and assess emergency medical care methods for heart attack victims and to develop and assess prophylactic treatment with drugs to prevent sudden cardiac death.

Following heart attack or other manifestation of heart disease, tens of thousands of Americans annually are left with substantial impairment of their ability and freedom to function within their capacity and to contribute fully to American society.

Prior clinical and fundamental research has provided knowledge of the causes, diagnosis, and treatment of coronary heart disease. This work is the basis upon which targeted research efforts can now be mounted.

In addition to topics identified under Coronary Heart Disease, closely related work is included in the sections on Arteriosclerosis, Arrhythmias, Heart Failure and Shock, and in the section on Prevention, Control, and Education Programs.

Opportunities and needs

The emphasis upon patient-oriented research must shift from a focus upon acute heart attack to the inclusion of other important aspects of the coronary heart disease - angina pectoris, heart failure, arrhythmias, and sudden death. Particular attention must be paid to further development and evaluation of therapy, rehabilitation, and measurement techniques suitable for use in patients. The fundamental question of why chronic coronary heart disease is finally manifested as heart attack or sudden death must be answered. The study of susceptible patients requires specialized facilities that are complex, expensive, and staffed with personnel who are available for emergencies. Importantly, such specialized cardiological facilities will be very useful for research on other forms of heart disease.

It is widely recognized that coronary artery surgery brings relief of symptoms for a majority of patients with angina pectoris. However, its benefits and side effects, its value compared to conventional drug therapy, and its effects upon life span and quality of life require further research.

Recent research has shown that the final step in sudden cardiac death is usually ventricular fibrillation, a chaotic disturbance of the heart rhythm. This rhythm disturbance is largely preventable during hospitalization by drugs given intravenously. Thus, the importance of finding drugs to prevent ventricular fibrillation in high risk patients is obvious. Agents must be found that can be used immediately upon the development of symptoms of heart attack.

The high frequency of out-of-hospital deaths and the favorable experience with improved systems of emergency cardiac care underscore the need for further development of emergency-related techniques and resources for use in cardiac patients.

Substantial efforts are now being directed at rehabilitation programs. However, a strengthened scientific basis for such programs and a more comprehensive scope of action are needed.

Development and testing of new hypotheses and methods are critical to continued clinical and fundamental research into the cause,diagnosis, and treatment of coronary heart disease.

Actions

To meet these needs and to explore the identified opportunities, the Institute will:

- Establish approximately 12 specialized units to conduct research upon the various manifestations of coronary heart disease. Comprehensive clinical investigations will be supported by related, fundamental laboratory studies.

- Establish a collaborative national program to determine the indications for and the long-term effects of coronary artery surgery in the management of coronary heart disease. Randomized studies will be utilized in patients with sharply defined clinical conditions and coronary arterial involvement. A registry will be used to follow patients in whom the indications for surgery or exclusively medical treatment seem sufficiently clear that randomized allocation would be improper, but in whom follow-up clinical data are important for assessing the validity of present clinical judgments.

- Implement the US-USSR cooperative study on the management of ischemic heart disease by medical and surgical techniques.

- Promote studies to elucidate the mechanisms and factors which precipitate acute coronary events and to determine the characteristics of individuals at highest risk for these events.

- Promote studies on the preliminary symptoms of acute coronary events and of patients' reactions and coping behavior in this setting with a view toward earlier diagnosis and treatment.

- Develop and test techniques of emergency cardiovascular diagnosis and therapy suitable for incorporation into emergency medical care systems.

- Design, pilot test, and subsequently implement large-scale trials of chronically administered antiarrhythmic drugs in patients at high risk for sudden cardiac death.

- Design, pilot test, and subsequently implement large-scale trials of the early administration of prophylactic antiarrhythmic drugs immediately upon the development of heart attack symptoms.

- Assess the needs and opportunities for cardiac rehabilitation in terms of physical, psychological, and societal factors, and implement appropriate programs of research.

Recent advances and progress

Plans for Specialized Centers to conduct research upon the various manifestations of coronary heart disease have been developed. A solicitation has been released and review of over 50 applicant centers is in progress. Phase I of the Collaborative National Study on Coronary Artery Surgery is essentially completed. Phase II has begun with the final definition of program objectives, formal protocol documents, and forms. The US-USSR Cooperative Study is maintaing its schedule. The results of present studies on mechanisms and factors precipitating acute cardiovascular events and their prodromata are under final stages of review. Pilot testing on antiarrhythmic drugs to be given to patients following hospitalization for acute myocardial infarction is progressing satisfactorily. The studies for early administration of prophylactic antiarrhythmic drugs in the emergency care setting has begun but is proceeding slowly. A task force has been established to assess the needs and opportunities for the physiological, psychological and societal rehabilitation of patients with cardiovascular disease.

Congenital and Rheumatic Heart Diseases

Program goals

The earliest surgical successes in the treatment of heart diseases were in the correction or palliation of congenital heart disease. These successes are being expanded in the development of diagnostic and surgical techniques applicable to the newborn. Important insights have also been gained into the development of the cardiovascular system.

- The major goals of the program are to understand better the causes of congenital heart disease, to improve diagnosis and therapy, and to rehabilitate patients with congenital heart disease, particularly the newborn.

Rheumatic heart disease is an immunological disturbance that frequently occurs years after initial rheumatic fever and prior streptococcal infection. Improved understanding and control of immunological problems could thus be important in the identification of susceptibility and the prevention of rheumatic heart disease, as well as in the success of cardiac transplants and in the prevention or treatment of cardiomyopathy and possibly other forms of heart disease.

- Another important goal is to attain a better understanding of the immunological problems associated with heart diseases.

Opportunities and needs

Essential to the prevention of congenital heart diseases is a better understanding of causes and of the normal development of the cardiovascular system.

The National Heart and Lung Advisory Council has recommended that the Institute conduct an "intensive interdisciplinary study of all aspects of the etiology and pathophysiology of congenital heart disease and the neonatal cardiovascular system". The roles of maternal infection and toxic exposures are particularly relevant. The emphasis on diagnosis, therapy, and rehabilitation of congenital heart disease patients must increasingly involve the newborn as well as school age children.

The roles and nature of immune mechanisms as they relate to the heart need to be better understood. Therapy for the suppression of harmful immunological responses must be developed and evaluated.

Clinical and fundamental research relevant to causes, diagnosis, and therapy of congenital heart disease, rheumatic fever, and rheumatic heart disease must be continued with periodic updating for approaches.

Actions

To meet these needs and to explore the identified opportunities, the Institute will:

- Develop research to emphasize such topics as cardiovascular development, as well as improved diagnostic techniques and therapy, particularly in the newborn.

- Establish a targeted effort to study immunological problems in heart disease and their management, specifically in relation to rheumatic heart disease, cardiac transplantation, and cardiomyopathies.

Recent advances and progress

There has been a continuing overall effort in the non-targeted areas upon the problems of congenital and rheumatic heart disease. There will be a diminished emphasis on the hemodynamic and surgical aspects of these diseases in older children and adults. The continuing and new actions will emphasize the causes of both congenital and rheumatic heart diseases. In coordination with the National Institute of Child Health and Human Development, the National Heart and Lung Institute will give special attention to the role of infections, drugs, and other toxic exposures during pregnancy in congenital heart disease. For congenital heart diseases, there will be an increasing clinical emphasis on the neonatal period.

Peripheral Vascular Diseases

Program goals

Peripheral vascular diseases are the cause of considerable suffering and disability. Surgeons have developed techniques to replace diseased peripheral artery segments with vascular or prosthetic grafts. Otherwise, peripheral arterial disease has been the focus of only a limited research effort, and peripheral venous disease and disorders of the lymphatics have received even less emphasis.

- The goals of the program are to improve diagnosis, therapy, and rehabilitation, and to improve understanding of the mechanisms causing peripheral arterial and venous diseases.

Opportunities and needs

Methods must be developed for diagnosing peripheral vascular diseases before they reach an advanced state, for more effective medical management, and for extending surgical therapy to small vessels. Understanding the basic cause of the diseases is most important and will require study of the role of neural control of vascular tone, mechanism of action of smooth muscle, pathogenesis of peripheral atherosclerosis, and the importance and significance of risk factors.

Actions

To meet and to take advantage of the opportunities to improve the management of peripheral vascular diseases, the Institute will:

- Encourage clinical, laboratory, and epidemiological research into the causes, diagnosis, and treatment of diseases of the peripheral arteries, veins, and lymphatics.

Recent advances and progress

Some epidemiological data on the prevalence, incidence, and potentiality of risk factors are being obtained from prospective population studies. Continuing and new actions on peripheral vascular diseases will emphasize clinical and basic investigation. Emphasis will be on diagnostic techniques for small vessels, and the relation of physiology and pathophysiology to clinical manifestations of disease. Multidisciplinary approaches will be emphasized as well as specific approaches.

Cardiomyopathies and Infections of the Heart

Program goals

Cardiomyopathies and infections of the heart are being recognized with increasing frequency. The importance of toxic substances, viral infections, and immunological phenomena is widely recognized, although a number of causes remain unknown. The advent of antibiotics has substantially diminished heart disease caused by bacterial infections. However, new problems have arisen, such as infections of prosthetic heart valves.

- The goals of the program are to prevent, diagnose, and treat the various cardiomyopathies and infections of the heart, with particular emphasis on improved understanding of their causes.

Opportunities and needs

There is particular need to understand the causes of cardiomyopathies and myocarditis. The roles of toxic substances, including drugs and alcohol, and of viral infections, and genetic disorders need to be investigated. Cellular and subcellular biochemical and immunological studies offer opportunities of improved understanding of these problems. Better diagnostic and therapeutic approaches to these diseases must be developed. Since these diseases stem from a variety of causes, research efforts need to be broadly based and involve multiple disciplines.

Actions The Institute will:

- Focus attention on studies of the etiologies of cardiomyopathies and infections of the heart, emphasizing epidemiological methods, viral and immunological research, the development and utilization of animal models, and the determinations of mechanisms of myocardial damage by application of biochemical, physiological, physical, and pharmacological techniques.

Recent advances and progress

Developments have taken place through the non-targeted programs.

Arrhythmias

Program goals

Important new concepts are developing about the correlation of electrical signals from the heart and diseases of the heart. New and important correlations are being made between electrocardiographic findings and the extent, severity, and even prognosis of heart disease.

Important concepts are developing about the different causations of arrhythmias and their differential responses to drug therapy. Most of the drugs currently most effective in the treatment and control of arrhythmias have side effects which limit their applicability.

- A major goal of the program is to develop methods for the prevention of arrhythmias which cause sudden cardiac death.

Identification of arrhythmias that carry a high risk of sudden cardiac death is fundamental to preventive measures. The analysis of spontaneous rhythms and the influence of drugs must be assessed by quantitative analysis of extensive electrocardiographic tape recordings. Substantial progress has been made toward performing this task automatically, rapidly, and quantitatively by computer.

Arrhythmias and other electrical disturbances of the heart cause important symptoms and aggravate many forms of heart disease.

- Another important goal of the program is to improve currently available methods for prevention, diagnosis, and management of arrhythmias and other electrical disturbances of the heart.

Opportunities and needs

Improved understanding of the electrical behavior of ischemic heart muscle is essential to the prevention of sudden cardiac death. Several drugs which are effective agents in the setting of the coronary care unit need to be evaluated for benefits and side effects as prophylactic agents outside the hospital in patients suspected of having myocardial infarction. Particular attention needs to be paid to the effect of heart rate and rhythm disturbances as well as upon the workload and consequent potential damage to the heart. Drugs having antiarrhythmic actions, which can be taken orally over long periods of time, and which have shown promise in limited clinical trials, need to be evaluated in larger scale trials.

Fundamental to all these clinical studies is the development of systems for quantifying electrocardiographic rhythm signals automatically and rapidly.

In addition to the efforts focused upon ventricular fibrillation and the prevention of sudden cardiac death, disturbances of the conduction system of the heart, as well as other important rhythm disturbances, must be managed more effectively.

Actions

To meet these needs and to explore emerging opportunities for the control of arrhythmias, the Institute will:

- Expand current programs for the prevention of arrhythmias causing sudden cardiac death, focusing particularly upon the electrophysiology and therapy of rhythm disturbances associated with inadequate blood supply to heart muscle and upon clinical studies to identify chronic or intermittent disturbances of heart rhythm which indicate a heightened risk of sudden death.

- Augment the development of automated, quantitative techniques for analyzing electrocardiographic rhythm signals to facilitate clinical investigation of arrhythmias.

Recent advances and progress

Clinical studies to identify chronic or intermittent disturbances of rhythm and several projects primarily directed at the electrophysiology and therapy of rhythm disturbances associated with inadequate blood supply to the heart are in progress. The development of a collaborative study is in progress to describe significant arrhythmias in specific groups of patients and their modification by drug therapy. Improved automated arrhythmia analysis of electrocardiographic records is taking place.

Cardiac Failure and Shock

Program goals

In heart attacks, blood supply to a part of the heart muscle becomes so severely reduced that the muscle undergoes irreversible damage. It can no longer contract or pump, and is ultimately replaced by scar. The amount of irreversibly damaged muscle is not predetermined at the onset of the heart attack; there is a zone which is in jeopardy but has not yet progressed to the point of no return. Current research has identified several promising means for protecting this zone of potentially reversible damage and for promoting its recovery. Some of these approaches are now at the stage of initial clinical feasibility trials; other promising techniques are still at the stage of animal studies.

- A major goal of the program is to minimize heart failure associated with and following heart attack by enhancing the survival of damaged heart muscle.

Methods of quantifying the amount of heart muscle which is inadequately nourished and therefore functioning poorly or which has undergone irreversible damage are crucial to the evaluation of therapeutic interventions. Recently, several such methods have shown promise. They may make it possible to test new approaches more economically and in fewer patients than is now required for evaluation by gross clinical criteria.

- A goal of the program is to develop more satisfactory means of quantifying the extent of heart muscle which is inadequately nourished with arterial blood or which has undergone irreversible damage.

Present and foreseeable techniques of general and pharmacological management of heart failure and shock still leave a substantial fraction of patients with compromised or fatally impaired heart failure. By mechanical supportive means, it is possible to substitute some of the pumping function of the heart and to relieve the burden of the heart. Presently such techniques are possible briefly in man and for longer periods in the experimental animal.

- A goal of the program is to develop and assess therapeutically effective, safe, and reliable cardiac assist and total replacement heart devices for supporting or taking over the workload of the heart.

Methods for assessing and quantifying the degree of circulatory impairment are essential in evaluating patients with all forms of suspect or known heart disease and particularly for patients with heart failure and shock.

- A goal of the program is the development of the instrumentation and techniques for the assessment of cardiovascular performance.

Other aspects of the diagnosis, etiology, therapy, and prevention of heart failure and shock warrant emphasis. These include research on improving the pumping action of heart muscle, as well as understanding and treating the disturbances of the regulation of peripheral blood vessels, the related endocrine functions of the body, and the functioning of the kidney.

- A goal of the program is the improved understanding and management of heart failure and shock due to cardiovascular causes.

Opportunities and needs

Current therapy to enhance the survival of poorly nourished heart muscle must be evaluated on a larger scale by more definitive clinical studies than those now underway. The amount of heart muscle damaged must be quantified and survival assessed. Inadequately nourished heart muscle must be studies at the cellular and subcellular levels, in an effort to determine new ways of supplying blood to the heart.

The techniques for quantifying the degree of heart muscle damage must be validated. Subsequent use of those found best would minimize the number of patients needed for evaluation of new modes of therapy. Electrocardiographic, enzymatic, and radioisotope techniques show promise.

Mechanical techniques for augmenting or substituting for the performance of the heart must be expanded. This is to encompass emergency temporary devices for short-term management, long-term implanted heart assist devices, and total cardiac replacements; there is an associated requisite opportunity and need for research on the physiology of assisted circulation, as well as the development of the requisite components of the systems - compatible biomaterials, pumps, actuators, energy transforming devices, implantable energy systems, transcutaneous transmission of energy, and the control system for the devices.

Studies of heart failure and shock need to be expanded to include other organ systems. Thus, as the National Heart and Lung Advisory Council has recommended, the dynamics and the neural and endocrine control of the circulation must be studied in the periphery as well as in the heart, kidney, and other organs.

Actions

To meet these needs and to explore the opportunities, the Institute will:

- Enlarge biochemical and physiological studies of the fundamental processes associated with heart muscle survival both in laboratory and clinical studies. Based upon these studies, develop methods for minimizing the extent of heart muscle damage in a heart attack.

- Establish clinical studies, contingent upon success of current pilot studies, to assess the therapeutic efficacy of promising techniques for minimizing the extent of heart muscle damage.

- Expand the program for quantifying the extent of heart muscle which is inadequately perfused or which has undergone irreversible damage.

- Continue the research, development, and assessment of emergency temporary, circulatory support devices directed at short-term management of heart failure and shock to stabilize the clinical condition and permit its reversal.

- Expand the research, development, and assessment of implantable heart assist devices for permanent implantation.

- Expand research and development upon circulatory assist and artificial heart systems, including the development of compatible biomaterials, appropriate pumps, actuators, energy transforming devices, implantable energy systems, transcutaneous transmission of energy, and control systems for these devices.

- Expand research and development on non-invasive and invasive instruments and techniques for the assessment of cardiovascular performance.

Recent advances and progress

Existing activities are continuing on the biochemical and physiological studies fundamental to the survival of heart muscle and to the development of methods to prevent heart muscle damage. Pilot studies with a variety of therapeutic agents are underway. Progress is being made in the development of radioisotopic techniques that quantify how much of the heart muscle has been damaged.

Other Heart and Vascular Diseases

National Research and Demonstration Centers

Section 415 of the National Heart, Blood Vessel, Lung, and Blood Act of 1972 authorizes the establishment of centers for basic and clinical research into, training in, and demonstration of, advanced diagnostic, prevention, and treatment methods, including methods of providing emergency medical services, in heart, blood vessel, lung, and blood diseases. The Act authorizes as many as fifteen such centers for heart, blood vessel, and blood diseases, and fifteen for lung diseases.

Such centers will be able to promote the effective and rapid translation of research advances into the realities of health care. It is requested that several centers be funded in 1975 and that sufficient time be permitted for careful review and evaluation of the strength and weaknesses of the program before funds for the full number of authorized centers are requested.

Prevention, Education, and Control

The overall goal of prevention and control programs is to develop and demonstrate effective means for the promotion of health, prevention of the heart and vascular diseases, early detection and treatment of those diseases and restoration of health.

The overall goals of the education and information programs are to:

- Make the public aware of the magnitude of these disease problems, the associated risk factors and available methods of therapy.

- Keep the health professional community abreast of new information and techniques and, thereby, also facilitate the flow of modern therapy and information on heart and blood vessel diseases to the public.

- Expedite the translation of basic research findings to their application as patient care principles.

Considerable knowledge is already available for the prevention and control of heart and blood vessel diseases. However, the most effective means to achieve application of this knowledge to individuals in need of such measures will require more specific research and evaluation efforts. The prevention and control programs should therefore seek immediate application of presently available knowledge for prevention and control while at the same time strive to make prevention and control measures more effective.

Particular emphasis should be placed on the testing and evaluation of a program for the prevention of the two major cardiovascular diseases--hypertension and arteriosclerosis. In these diseases, a sufficient base of knowledge exists which could result in substantial reductions in morbidity and mortality if implemented through coordinated, comprehensive programs. Prevention or amelioration of the consequences of other cardiovascular disease will also require attention in planning the National Program.

Activities in the areas of hypertension and arteriosclerosis are already underway. Activities in coronary heart disease and congenital heart disease are now planned initiatives.

Drug therapy to control blood pressure reduces the incidence of strokes and heart failure among persons with moderate and severe hypertension. However, only about 12 percent of hypertensives are currently receiving adequate treatment. Immediate efforts to expand current program initiatives through existing medical networks are urgently needed to bring individuals with moderate and severe hypertension under effective treatment. Sustained effective blood pressure management in such persons should result in a reduction of disability and mortality of as much as 40 percent when compared with expected rates for untreated hypertension.

- A national goal of the program is to motivate all adults to have their blood pressure checked annually and for those found to be hypertensive, to urge them to obtain proper therapy.

- A further national goal is to have current knowledge of antihypertensive drug management available and effectively practiced by the general practitioners as well as the specialists from whom the individuals with high blood pressure seek therapy.

The National High Blood Pressure Education Program initiated in 1972 has completed the preliminary studies of the needs of the program and the Hypertension Information and Education Advisory Committee has submitted its recommendations to the Secretary. Implementation of some recommendations that arose from immediately recognizable needs are in the planning phase or already initiated.

In the Hypertension Detection and Follow-up Program a broad range of over 5,000 hypertensive patients from 14 communities of all races and several ethnic groups, men and women, are participating in a treatment program. About one-third are blacks, including rural and inner city groups. Special educational efforts to encourage patients to attend clinics and take their medication regularly are being undertaken.

A number of factors have been identified that increase susceptibility to atherosclerosis and coronary heart disease. These include elevated blood lipids, high blood pressure, and cigarette smoking. These risk factors can be modified and the public needs to know how this can be done. Program goals are to:

- Reduce disability and death from arteriosclerotic disease of the blood vessels to the heart, brain, and extremities through the prevention and control of risk factors.

As discussed previsouly in Coronary Heart Disease, emergency medical care for the person with suspected heart attack is a major problem, since there are about 400,000 deaths from coronary heart disease prior to hospitalization.

- A goal of this control program is to introduce the developments in emergency medical care for the cardiac patient into comprehensive emergency care systems.

- An additional goal is to conduct research on improved methods for cardiac rehabilitation.

The recognition of congenital heart disease is particularly difficult in the newborn period. Yet this is the period where a substantial fraction of deaths from congenital heart disease occur.

- The goal of this control program is to recognize and manage congenital heart disease in the newborn.

Lung Diseases

	1974 Base *		1975 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits	---	---	---	---	---	---
Other expenses	---	$37,906,000	---	$45,340,000	---	+$7,434,000
Total	---	37,906,000	---	45,340,000	---	+7,434,000
Subactivities:						
Structure and Function of the Lung	---	5,937,000	---	6,628,000	---	+691,000
Pediatric Pulmonary Diseases	---	5,041,000	---	6,793,000	---	+1,752,000
Emphysema and Chronic Bronchitis	---	8,677,000	---	9,888,000	---	+1,211,000
Fibrotic and Immunologic Lung Diseases	---	3,534,000	---	3,946,000	---	+412,000
Other Lung Diseases	---	12,257,000	---	15,685,000 1/	---	+3,428,000 1/
Prevention, Education, and Control	---	100,000	---	550,000	---	+450,000
Research Manpower Development	---	2,360,000	---	1,850,000	---	-510,000
Total	---	37,906,000	---	45,340,000	---	+7,434,000
Budget Mechanism:						
Research Grants:						
Regular	---	27,320,000	---	34,418,000	---	+7,098,000
Special	---	1,939,000	---	2,270,000	---	+331,000
Subtotal	---	29,259,000	---	36,688,000	---	+7,429,000
Fellowships	---	732,000	---	1,410,000	---	+678,000
Training Grants	---	1,628,000	---	440,000	---	-1,188,000
Research & Development Contracts	---	6,287,000	---	6,802,000	---	+515,000
Total	---	37,906,000	---	45,340,000	---	+7,434,000

1/ Includes Research & Demonstration Centers for multi-categorical lung disease research.

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* Excludes 1973 appropriation restorations.

Objectives, 1975

An increase of $7,434,000 above amounts available for obligation from 1974 appropriated funds (exclusive of the effect of 1973 released funds) is requested for 1975 to support regular research grants at essentially the 1974 level ($1,670,000); expand the Specialized Centers of Research program, particularly in pediatric pulmonary diseases ($2,128,000); establish perhaps 2 Pulmonary Research and Demonstration Centers ($2,000,000); launch programs through grants and contracts in pulmonary prevention, education, and control ($450,000); expand the Pulmonary Young Investigator Award program ($1,000,000) and the Pulmonary Academic Award program ($331,000); and expand research contract programs, with some divergence of funds to support animal models on Sarcoidosis and place increased emphasis on pediatric pulmonary diseases and on emphysema and chronic bronchitis ($365,000). There would be a net decrease of $510,000 in research manpower development programs as a result of the phase-out of graduate pulmonary training grants as presented to the Congress last year. Assistance to graduate students and post-graduates in the life and social sciences will be more equitably provided under the expanded general assistance programs available to all graduate students through the Office of Education. There are, however, certain identifiable research manpower needs relevant to particular areas or disciplines, fields, or specialties. To meet these needs the NIH is to implement a new fellowship program this year, which was announced by Secretary Weinberger on July 9, 1973, and which has excited wide interest in the biochemical research community. Funds in 1975 will provide for specifically identified research manpower needs in lung structure and function, biochemistry, metabolism, biophysics, cell biology, immunology, and bioengineering.

Accomplishments and Objectives 1973/1974

In 1973 the Division of Lung Diseases supported pulmonary research grant programs at a level of $20,000,000, an increase of about 18 percent over the prior year and 50 percent above the level of 1971. These increases are reflected in some substantive changes in the program's emphasis, changes that are responsive to the need for additional attention to some diseases and approaches that have been identified as important to national health. In meeting these needs, the Division's programs have expanded in both investigator-initiated and targeted research.

Two contract proposals were issued in 1973, one on extracorporeal support for respiratory insufficiency and the other on normal lung cell separation culture and morphology. Environmental diseases of the lung are receiving increasing emphasis, especially with regard to the effects of cigarette smoking.

Investigator-initiated research grants and program projects now represent 58% of the Division's support for pulmonary research; about $3,000,000 more than the prior year. Contracts, which represent 12% of the Division's research support, increased by about $900,000. Support for Pulmonary Specialized Centers of Research is essentially unchanged as there has been no competition for new centers since the last fiscal year.

The Division also supports a targeted research program: the Pulmonary Academic Award. Designed to attract bright young physicians into careers in pulmonary medicine or pulmonary research, this program has been a great success. Presently 16 Pulmonary Academic Awards are being funded.

Structure and Function of the Lung

Program goals

Past pulmonary research has focused on studies of the respiratory physiology of the lung. While this has provided a basis for diagnosis, it has not contributed to our understanding of disease etiology and mechanisms. A better understanding of lung tissue biology would lead to major advances in combating emphysema, chronic bronchitis, pulmonary fibrosis, immunologic lung diseases, respiratory distress of children, and respiratory failure.

- While is it essential to first focus studies on the cellular biology of the normal lung, the ultimate goal of the program is to increase understanding of the disease processes and to develop effective methods for prevention, diagnosis, and therapy of lung diseases.

Opportunities and needs. An expanded emphasis on studies of the basic structure, function, and metabolism of the lung are needed at this time. These studies should include the quantities, composition, and mechanisms of development of the various components in normal lung tissues, their chemical precursors and their possible variations with age, sex, and environmental influences. It is not known how variations in structural proteins, lipids, and hormones are involved in diffuse pulmonary fibrosis and in various types of obstructive disease of the airways. The in vivo balance and interaction among proteolytic enzymes need to be determined since they have potential for altering the connective tissue in the lungs.

Improved knowledge about the structure and function of the various cell types making up normal lung tissue is important, as loss and replacement of these cells play a major role in the development of many lung diseases. Measurements of turnover rates of lung cells and alterations in these rates with disease require further study. Ultrastructural investigations will play an essential role in the development of this information as will efforts to isolate and characterize individual cell types.

More needs to be known about the lung's defense mechanisms, since the failure of these may play an important part in disease processes. Bronchial mucus is one of the factors in the defense mechanisms of the lung. The structure, synthesis, physical and physico-chemical characteristics of this substance need to be elucidated. The cilia in the bronchial tree are another vital defense mechanism, and investigations of the structure and function of cilia are crucial in understanding lung clearance and host defense.

A number of classical areas of pulmonary physiology require continued study and correlation with new knowledge of cellular biology, structure and function. Ongoing physiologic studies focus on the mechanical properties of the lungs and the pulmonary blood vessels, and the coupling of mechanical events to the neurophysiological regulation of ventilation.

Actions. To meet these needs for increased information and to take advantage of the opportunities presented by modern investigative techniques, the Institute will:

- Encourage investigator-initiated research in metabolism, cellular biology, and defense mechanisms of the lung. This will be supplemented as needed by targeted research addressed to topics not adequately covered by investigator-initiated research.

- Develop multidisciplinary approaches, such as program projects or Specialized Centers of Research, in the area of normal lung structure and function. In addition, new types of targeted programs will be initiated for collaboration between fundamental and clinical disciplines. These broad-based programs will require the collaboration and exchange of information between basic scientists such as biochemists, immunologists, and cell biologists, who are not yet focusing on the lung, and pulmonary specialists who need to develop information in basic science areas.

Pediatric Pulmonary Diseases

Program goals

Among childhood disorders involving the lung, cystic fibrosis, and hyaline membrane disease are health problems of national significance. Respiratory distress syndrome (hyaline membrane disease) is the most common cause of death in the newborn in the United States, and affects between 50,000 and 100,000 babies each year, about half of whom die. Bronchiolitis is one of the major obstructive airway diseases of children and may be important in the development of adult chronic lung disease. The cause of respiratory distress syndrome of the newborn, the nature of cystic fibrosis, and the possible long-term effects of early childhood bronchiolitis need to be determined and understood.

- Until research has uncovered ways to prevent hyaline membrane disease, early diagnosis and prompt initiation of therapy are essential to save the lives of babies born with this disorder. Primary goals of this program are to develop improved methods for early diagnosis and to design more effective modes of therapy.

- Similarly, present modes of therapy for cystic fibrosis, a genetically determined disease, are at best palliative. The primary goal at this time is to develop a rational basis for therapy through an understanding of the pathogenesis of this disease.

- There is reason to believe that bronchiolitis in children may be related to chronic lung disease in the adult. Therefore, an important goal is to conduct long-term, follow-up epidemiologic studies of children who have had bronchiolitis.

Opportunities and needs. Two important breakthroughs have occurred in the detection and treatment of hyaline membrane disease. First, it is now possible to detect the disease before birth. Secondly, an important therapeutic breakthrough has occurred which dramatically reduces the mortality from this dreaded disease.

Survival of infants with hyaline membrane disease is usually determined within a matter of days to 1 to 2 weeks. Therapeutic efforts have focused on methods of keeping the airways patent and maintaining adequate oxygenation of the blood through artificial ventilation and other aspects of intensive care usually available in large hospital centers. Unfortunately, this was not sufficient and more than half of these infants died. A provocatively simple technique, albeit one that requires scrupulously attentive patient care, has resulted in survival of up to 90 percent of these babies. This therapy, known as continuous positive airway pressure (CPAP), is used in conjunction with artificial ventilation. With increasing acceptance of this exciting therapeutic, achievement by neonatal intensive care units throughout the country, the mortality due to this disease should be drastically reduced.

The clinical aspects of cystic fibrosis and its treatment as well as the underlying genetic and physiologic alterations are being investigated. Although this disease affects many organs, the pulmonary impairment which may be related to recurrent infections and abnormalities in mucus production commonly causes disability or death. The Institute's program is addressed to evaluation of cardiac and pulmonary functions and their alteration with therapy. The biochemistry of the mucus abnormality is also being investigated.

Several groups are engaged in research on methods for early diagnosis of airway disease in newborns and young children. A spirometer designed for compliance measurements in premature and term newborn infants is in the developmental state. A system which is designed to measure pressure-volume curves of the lung and thorax, and functional residual capacity in anesthetized subjects is also being evaluated. Investigators have initiated a long-term study of effects of viral lower respiratory tract illness in children on later development of adult lung disease. Serum alpha$_1$-antitrypsin (an enzyme) activity and serum antibody titers to common respiratory viruses are being measured in children with bronchiolitis.

Actions. The Institute plans to:

- Extend interdisciplinary studies of biochemical changes associated with hyaline membrane disease through Specialized Centers of Research. In addition, programs will be initiated to study biochemical changes associated with the development of cystic fibrosis.
- Test various supportive measures for patients with cystic fibrosis, including mist-tent therapy and bronchodilators.
- Improve management and therapy of hyaline membrane disease through the development of programs for rapid transfer of infants with this disease to intensive care units. Programs will be initiated for research and development of new or improved devices for treatment and controlled clinical trials of available methods of treating hyaline membrane disease and cystic fibrosis.
- Initiate epidemiologic studies to determine prospectively the long-term effects of bronchiolitis in childhood on the occurrence of chronic lung disease in the adult.

Emphysema and Chronic Bronchitis

Program goals

Research on emphysema and chronic bronchitis, which has focused chiefly on pathophysiology and pulmonary function testing, has not provided the needed information on disease causes, despite considerable gains in our ability to diagnose disease.

Association of these diseases with certain risk factors, such as cigarette smoking and in some cases with genetic determinants (e.g., alpha$_1$-antitrypsin deficiency) is strongly suggested. Furthermore, it is now believed that early abnormalities (physiologic, biochemical, etc.) related to emphysema and chronic bronchitis may be detected at a stage when lung damage is still reversible.

- Because of the nature of these disease problems, a goal of the program is to prevent development of these diseases by early diagnosis and identification and control of risk factors.
- At the same time, because of the great number of individuals suffering from already established and progressive disease, another goal is to improve treatment and rehabilitation programs.
- To understand the mechanisms and causes of these diseases is also an important goal and will be greatly aided by the development of basic knowledge of normal lung biochemistry, metabolism, response to injury and repair processes.

Opportunities and needs. Among presently identified risk factors, smoking plays a key role in the development of both chronic bronchitis and emphysema. We need to identify the factors in cigarette smoke that produce lung damage as a step toward reducing the injurious effects of tobacco on the lung. To understand the role of smoking, it is essential to study the mechanisms by which the lung clears itself of particles that are inhaled in cigarette smoke, how these mechanisms are modified by pollutants in the environment, and, through prospective epidemiologic studies, what determines individual differences in response to the harmful effects of tobacco. It is also important for us to investigate measures that will modify the smoking habits of the population.

Host factors, some genetic in origin, may be determinants of emphysema and chronic bronchitis. The association of inherited alpha$_1$-antitrypsin deficiency and the occurrence of emphysema suggests that other situations associated with accelerated enzymatic digestion of lung connective tissue may be implicated in emphysema. A systematic search for inherited enzyme abnormalities that predispose to development of obstructive lung disease is an essential part of a program on host factors.

There is need to develop improved techniques and devices to detect biochemical, immunologic, or physiologic abnormalities associated with emphysema and chronic bronchitis sufficiently early to effect reversal of the process, something now believed possible. If successfully developed, the next step would be testing such techniques for applicability in mass screening programs. Knowledge of risk and host factors and their control will be essential to successful intervention in the disease process. There is also a need for systematic evaluation of improved therapeutic and rehabilitative approaches.

Actions. To meet these research needs in emphysema and bronchitis and to explore opportunities for solutions, the Institute will:

- Develop a multidisciplinary program addressed to the problem of smoking. This program will include investigation of the mechanisms and agents responsible for cigarette smoke injury in emphysema and chronic bronchitis, as well as efforts to modify smoking habits by means of psychological and pharmacological approaches.

- Elucidate the role of host factors, including genetic ones, in the development of emphysema and chronic bronchitis by conducting and extending epidemiological studies.

- Enlarge efforts in emphysema and chronic bronchitis prevention through the development of improved techniques and devices for early detection of reversible diseases and application of new knowledge from studies of risk factors and their control. Epidemiologic screening studies may be required at a later date if this program proves successful.

- Initiate controlled clinical trials to evaluate the efficacy of current and newly developed approaches to therapy and rehabilitation.

Fibrotic and Immunologic Lung Diseases

Program goals

Fibrotic and immunologic lung diseases, induced by external agents (e.g., mold from hay), that can be prevented or treated by removal of the offending substances or suppression of their effects. Therefore, a primary goal of the National Program in this area is to disseminate information about the causes of these diseases and how to avoid them.

In cases where exposure cannot be avoided or the disease prevented, effective treatment depends on understanding the processes leading to disease.

- The research goal is to conduct fundamental investigations essential to the development of improved therapy.

Opportunities and needs. Where population groups are known to have a high prevalence of pulmonary fibrosis or immunologic lung diseases, epidemiological studies should be carried out to identify the factors responsible. This identification of specific etiological agents is crucial to the development of effective control measures.

Advances in biochemistry, pharmacology, and immunology need to be brought into the development of therapy, prevention, and control of immunologic and fibrotic lung diseases.

There is need to develop fundamental research on the mechanisms of collagen synthesis and degradation in order to develop therapy directed at specific events in the chain of metabolic events leading to disease.

Many animal models of immunologic and fibrotic lung diseases are available and represent opportunities for study of the pathogenesis of these diseases.

Actions. To meet the needs in fibrotic and immunologic lung diseases and to explore opportunities for solutions, the Institute will:

- Seek new information about the synthesis and degradation of collagen and the immunologic responses and defense mechanisms of the lung through continued and extended multidisciplinary programs. These will involve collaboration by immunologists, biochemists, physicians, and physiologists.
- Initiate programs to develop pharmacologic agents that will modify the alterations in connective tissue metabolism that lead to pulmonary fibrosis, and study the use of immunologic techniques to stimulate tissue defense mechanisms against immunologic diseases.
- Initiate epidemiologic studies to investigate etiologic factors in population groups characterized by unusual prevalence of fibrotic and immunologic lung diseases.
- Develop a program of education.

Prevention, Education, and Control

The major emphasis in prevention, control, and education in the lung diseases area will be on smoking control programs to decrease the problems of emphysema and chronic bronchitis. Other efforts include programs in pediatric pulmonary diseases, fibrotic and immunological lung diseases, and respiratory failure.

Emphysema and Chronic Bronchitis

Program goals

Cigarette smoking is believed to be a prime factor in the cause or exacerbation of chronic bronchitis and emphysema, and a contributing factor to environmental lung diseases, including pneumoconiosis and hypersensitivity lung diseases. Up to 20% of smokers have chronic obstructive lung disease and almost all patients with this disease are smokers. Extensive studies document conclusively that cigarette smokers are far more likely to develop emphysema than non-smokers. Also, once developed, it progresses much more swiftly in those who smoke. Repeated exposure to pollutants in the air also contributes to the development and progress of the disease.

The principal cause of chronic bronchitis is prolonged irritation of the bronchial tube linings. Smoking, air pollution and recurrent infections are the main irritants for chronic bronchitis, as well as for emphysema. The public needs to be informed about the potential seriousness of persistent or recurrent coughs and shortness of breath and about ways to protect against progression of this disease.

- The program goal is to modify the smoking habits of persons at risk of developing lung diseases, and to extend successful anti-smoking programs to the general population.

Opportunities and needs. To prevent or modify smoking habits in those at greatest risk, it is necessary first to identify persons likely to develop chronic obstructive pulmonary disease, especially those who have predisposing genetic characteristics.

There is also need to prevent or modify smoking in persons who live or work in environments with unusually high concentration of air pollutants, coal dust, or other environmental agents implicated in the development of lung diseases.

Sophisticated motivation approaches must be developed to modify the smoking habits of persons at risk and, in general, large population groups. Those who have not yet acquired the habit should be discouraged from doing so through effective educational programs.

Actions. To meet these needs, the Institute will:

- Develop a program, in collaboration with experts from other federal agencies, to modify effectively the habits of smokers.
- Develop an educational program to reach the lay public and alert it to the dangers of smoking in relation to chronic obstructive pulmonary diseases and environmental lung diseases, and urge smokers in populations at special risk to participate in programs to modify their smoking habits.

Pediatric Pulmonary Diseases

Program goals

About 40,000 babies are born each year with hyaline membrane disease. More than half of these will die unless given prompt treatment.

- Until hyaline membrane disease can be prevented the primary goal will be to initiate prompt diagnosis and therapy.

Action. The Institute will:

- Develop education programs, addressed to pulmonary and community physicians, to provide presently available information about treatment of hyaline membrane disease.

Fibrotic and Immunologic Lung Diseases

Program goals

Diseases that are induced by external agents can be prevented or treated by removal of the offending substances or suppression of their effects.

- A primary program goal is to disseminate information about the causes of fibrotic and immunologic lung diseases and how to avoid them.

Opportunities and needs. Wide dissemination of available knowledge about external agents implicated in the development of immunologic and fibrotic lung diseases should be provided to the lay public as well as to physicians.

Action. The Institute will:

- Develop a program of education of physicians and the lay public with regard to environmental agents implicated in pulmonary fibrosis and immunologic lung diseases.

Other Lung Diseases

Pulmonary Research and Demonstration Centers

The concept of these centers is discussed under Heart and Vascular Diseases.

Blood Diseases and Resources

	1974 Base *		1975 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits..........	---	---	---	---	---	---
Other expenses..........	---	$44,976,000	---	$50,309,000	---	+$5,333,000
Total.........	---	44,976,000	---	50,309,000	---	+5,333,000
Subactivities:						
Blood Diseases:						
Thrombosis & Hemmorhagic Diseases.......	---	15,316,000	---	17,318,000	---	+2,002,000
Sickle Cell Disease & Related Diseases.....	---	15,500,000	---	15,500,000	---	---
Other Blood Diseases..	---	4,226,000	---	5,778,000[1]	---	+1,552,000[1]
Blood Resources:						
Nationwide Blood System..............	---	396,000	---	448,000	---	+52,000
Safety of Blood Therapy.............	---	3,072,000	---	3,474,000	---	+402,000
Blood Component Therapy.............	---	4,389,000	---	4,963,000	---	+574,000
Transplantation Biology.............	---	204,000	---	231,000	---	+27,000
Other Blood Resources.	---	661,000	---	747,000	---	+86,000
Prevention, Education, & Control............	---	200,000	---	550,000	---	+350,000
Research Manpower Development..........	---	1,012,000	---	1,300,000	---	+288,000
Total..............	---	44,976,000	---	50,309,000	---	+5,333,000
Budget Mechanism:						
Research Grants:						
Regular.............	---	29,163,000	---	32,747,000	---	+3,584,000
Special.............	---	589,000	---	560,000	---	-29,000
Subtotal..........	---	29,752,000	---	33,307,000	---	+3,555,000
Fellowships...........	---	600,000	---	1,200,000	---	+600,000
Training Grants........	---	412,000	---	100,000	---	-312,000
Research & Development Contracts............	---	14,212,000	---	15,702,000	---	+1,490,000
Total.............	---	44,976,000	---	50,309,000	---	+5,333,000

1/ Includes Research & Demonstration for multi-categorical blood diseases and resources research.

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* Excludes 1973 appropriation restorations.

Objectives, 1975

Support will be given to continue the regular research grant program at a stable level, some expansion of the Specialized Centers of Research program may be accomplished, an initial effort in Research and Demonstration Centers will be launched, and an expanded research contract program will be accomplished.

Under the authority of the Public Health Service Act, Section 301, Title IV, Part B, and Title XI, this segment of the Institute

- Plans and directs the Institute's research grant, contract, and training programs in blood diseases and resources, including sickle cell disease, encompassing basic research, targeted research, clinical trials and demonstrations, technological development, and application of research findings.
- Maintains surveillance over developments in this program area and assesses the national need for research in the causes, prevention, diagnosis, and treatment of blood diseases, in technological development, in the application of research findings, and for manpower training in these areas.
- Conducts research and demonstrations to improve the national systems of blood procurement, management, and distribution.
- Coordinates Federal sickle cell disease activities, and operates a national clearinghouse for information on sickle cell disease.
- Maintains the necessary scientific management capability to foster and guide an effective attack upon blood diseases and for the management of blood resources.

The enactment by the Ninety-Second Congress of the National Heart, Blood Vessel, Lung and Blood Act of 1972 (Public Law 92-423) provides the Division of Blood Diseases and Resources with specific authority to undertake studies and research into blood diseases and blood resources, and to supervise the use of blood for clinical purposes as well as all aspects of the management of this resource. These activities include collection, preservation, fractionation, and distribution of blood and its products. In addition, under Public Law 92-294, this Division is responsible for the overall coordination of all Federal Sickle Cell Disease Programs including basic and applied research. Service activities such as the development of information and educational materials as well as the establishment of voluntary screening and counseling programs are funded.

Accomplishments and Objectives, 1973/1974

In March, 1973, the Blood Resource Branch began an in-depth study of four of the major problems relating to the nationwide blood system identified by an earlier report entitled "The Study of Blood Banking in America." As a result of these efforts, data necessary for the establishment of a national voluntary blood service are becoming available for the first time.

Efforts are continuing to develop a rapid, sensitive, specific screening blood test for hepatitis. In 1973, the Australian radio-immunoassay test was found to have less than ideal reproducibility. The hemagglutination inhibition test was successfully automated, but it was found to be unsatisfactory for routine blood bank use because of reagent expense required for testing. The reverse passive hemagglutination technique was found to possess greater sensitivity than current techniques. Additional studies to determine its reproducibility are to begin in 1974. During the past year, it has been found by *in vitro* assays that hepatitis B antigen can be removed from each of the major plasma fractions. Should this finding be verified in animals, its application would reduce the risk of hepatitis to patients dependent on blood concentrates. Additional work is continuing to define the epidemiology and to develop a practical test to identify virus carriers.

Techniques to extend the shelf life of platelets from 24 hours to 72 hours have been developed.

Research programs have also been initiated that will develop techniques for automatic blood typing, donor-recipient blood transfusion identification, as well as detection systems for Cytomegalovirus. Significant progress has also been made in improving and standardizing the preparation of cryoprecipitated anti-hemophilic factor, new methods of plasma fractionation and in exploring plastic bag toxicology.

Programs set up in 1972 to carry out the goals and objectives of the Federal Sickle Cell Disease Program were expanded. Fifteen comprehensive Sickle Cell Disease Centers are serving as a focal point for research and community service projects. Screening and Education Clinics have also been expanded to 26. This component of the program determines methods to stimulate public awareness and facilitate education, screening, counseling, and patient referral. Mission oriented research has developed several techniques that have allowed sophisticated studies of hemoglobin interaction, as well as automatic measurement of oxygen equilibrium curves. Basic research programs in other related areas of hemoglobin research such as Cooley's Anemia are proceeding. Major emphasis is directed toward an understanding of pathogenetic mechanisms.

A major portion of this activity's programmatic effort is directed toward basic research in understanding the fundamental mechanisms of hemorrhagic and thromboembolic disorders. In 1973 methods for determining hyper-coagulable states were identified, several thromboresistent surface materials were developed and alterations of blood components during thrombosis were investigated. The Urokinase Streptokinase Pulmonary Embolism Trial was completed.

Bleeding and Clotting Disorders

The Hemophilias

The hemophilias represent striking examples of diseases in which basic and clinical research have led to advances that have revolutionized patient care. Laboratory research in the 1950's and 60's first provided conclusive evidence that what appeared genetically and clinically to be a single disease in actuality resulted from a deficient activity of either one of two different clotting proteins (called factors VIII and IX) which are entirely different.

- A major research goal of the hemophilia program is to improve the methods for preparing the missing factors so that they can be made available to all who need them at reasonable cost.

Platelet Abnormalities

In the mid 1960's, new interest developed in the role of blood platelets. Today, rapid progress is being made in this area. Recent studies suggest a broad biologic role for platelets including involvement in disorders of the microcirculation, in the development of atherosclerosis, and in certain types of host-defense reaction. Nevertheless, details of their functions and how they can be manipulated to benefit the patient remain poorly understood.

- The goal of this program is to determine the role of platelets in thrombosis and hemorrhage.

Microcirculatory Thrombosis

As indicated earlier, bleeding and clotting with the microcirculation play a role in many disease states. Consequently, improved understanding of the microcirculation offers an enormous opportunity for better health maintenance.

- The goal of this program is to understand better the microcirculation and the systemic effects of bleeding and clotting within this system.

Thromboembolism in Relation to Prosthetic Devices

The only truly nonthrombogenic (clot-resisting) material known today is the lining of normal blood vessels. The development of nonthrombogenic artificial materials requires special emphasis because such surfaces would provide the key to the development of a whole range of diagnostic and therapeutic devices. At present, artificial devices can be used only if the period of contact with the blood is short; if their surface area is very small, as with heart valves; if the risk of thrombosis is accepted, as in vessel grafts; if the surfaces are constantly washed clean in areas of high fluid flow, such as intra-aortic balloons; or if their use is supplemented by drugs that inhibit clot formation, such as heparin in cardiopulmonary bypass or in hemodialysis. Because no truly nonthrombogenic artificial materials are available today, the impressive surgical advances in replacement of sections of diseased blood vessels and heart valves and production of functioning artificial kidneys and heart-lung machines cannot be fully exploited.

- The goal of this program is to study the blood vessel lining, hematology and hemodynamics, and to develop nonthrombogenic materials, both living and nonliving, suitable for use in prosthetic devices.

Thromboembolic Disorders

The approaches to both venous and arterial thromboembolism share two important concepts: (1) their causes involve an interplay of the blood coagulation system, the platelets, the vessel lining and the properties of flowing blood, and (2) application of previously accumulated and newly generated knowledge in these areas can be expected to provide health benefits to a large number of American people.

- The goal of this program is to facilitate detection and treatment of thromboembolic disorders by development of techniques and evaluation of drugs.

Sickle Cell Anemia and Sickle Cell Trait

The research goals of the sickle cell disease program are to develop improved therapy for sickle cell crises; increase knowledge of the fundamental biology of the disease and its complications; and develop effective and acceptable methods for screening and counseling.

Cooley's Anemia and Related Hemoglobin Variants

There is need to develop a simple screening technique to identify carriers and to determine the prevalence of the disease; develop improved treatment methods, preferably ones that would obviate the need for frequent transfusion; and increase fundamental knowledge regarding control of synthesis of the hemoglobin molecule with a view toward achievement of preventive measures.

Red Blood Cell Membrane and Enzyme Systems

Compared with other body cells, red blood cells are easily obtained and readily studied. Their metabolism is complex and specialized; yet, it is simple compared with the metabolism of other body cells and shares enough common features to serve as a useful model. Thus, clues obtained in red blood cells regarding metabolic controls and regulation may be expected to have wide applicability for understanding other, less accessible, body cells.

- The goal of this program is to learn as much as possible about membrane structure and function and intracellular metabolic activity. Such knowledge will contribute toward control, treatment, and prevention of the specific diseases. High yields in all of medicine can be expected from application of this knowledge to other, inaccessible cell systems.

Blood Resources

Scientific advances must be applied to increase the quality and number of blood products available. Managing the national blood resource requires a combination of human resources, sociologic, economic, scientific, medical, and management expertise, and technology, instrumentation, and manufacturing capabilities. The blood service complex has provided essential services and products; it has not consistently maintained an adequate supply or achieved the highest attainable quality of blood therapy.

- The goal of this program is to achieve an adequate supply of high quality blood and blood components by utilizing the national blood resource with maximal efficiency, economy, and safety.

Nationwide Blood System

The present complex by which blood and blood products are provided to the American people is fragmented, inadequately regulated, unplanned, and poorly managed. The result is inefficient use of resources and a compromise in quality and safety. What is known often has been applied slowly and sometimes not at all. Despite these serious shortcomings, the complex has enormous strengths and, in the main, has served the American people well. Present needs are to:

- Develop and promulgate a National Blood Policy which establishes the goals of a nationwide blood system, specifies the steps to achieve these goals, and provide a framework for building a pluralistic system, relying on existing resources whenever possible.

- Establish data and information systems on all aspects of blood banking, including cost-charge relationships, in order to evaluate the performance of the system and to design necessary changes therein.

- Employ the full regulatory authority of the Food and Drug Administration to enhance the quality and effectiveness of the national blood supply.

Safety of Blood Therapy

In spite of rapid advances in the understanding of hepatitis, including serum hepatitis, there is still no way to ensure that blood from a given donor will not transmit the disease. Cytomegalovirus disease is also emerging as a major cause of death in transfused patients whose immune mechanisms are depressed. The role of the blood donor in transmitting cytomegalovirus must be elucidated, and means of prevention developed and implemented. Histocompatibility antigens transfused in blood may make further transfusions useless if the recipient becomes sensitized to them. Means of removing such antigens need to be developed. Human error in matching donor and recipient remains a major hazard in transfusion therapy and fail-safe systems need to be developed and applied.

If human error is eliminated, retransfusing the patient's own blood constitutes the safest form of transfusion therapy. Means to develop further this form of therapy, termed autotransfusion, both by having the patient bank his blood prior to need, and returning blood lost during surgery to him, must be explored. In addition to increasing safety, this form of therapy might be expected to reduce significantly the demand on the nation's blood resources.

Blood Component Therapy

The medical demand for red blood cells, as distinguished from other blood components, sets the pace for the collection of whole blood. Patients who need red cells often do not need the other components. Currently, whole blood is used in more than three-fourths of all transfusions; experts indicate the whole blood is needed in less than one-fourth of cases. Reducing the use of whole blood not only constitutes good medical practice, but increases the availability of components often in short supply and needed by others. For example, factor VIII and factor IX concentrates are needed to control hemorrhage in hemophilia; gamma globulin can prevent many infectious diseases even if given after exposure; platelets can restore the ability to clot if the patient's platelet production is impaired. Optimal utilization of the nation's blood resource requires:

- Better methods of blood cell separation and preservation and of plasma fractionation so that the many important components can be recovered efficiently and economically.

- Clearer indications for the use of individual components and better methods to assess their effectiveness.

Hepatitis

A substantial portion of funds available for blood resources in 1975 will be used to expand hepatitis programs to support new epidemiologic research, research on the immunology of hepatitis, new studies to remove or inactivate all the infectious agents in blood, and research to develop hepatitis-A tests.

Transplantation Biology

The concept of transplantation of vital tissues is a natural extension of the transfusion of blood and blood products. Similar genetic and immunologic principles apply, and, indeed, many of the problems of finding the best kidney for a particular recipient are not unlike those of providing the most suitable blood for transfusion. While already experiencing many breakthroughs, tissue transplantation is still in its infancy, and much remains to be done. The Institute plans to significantly expand this type of support in 1975.

Other Blood Diseases and Resources, Research and Demonstration Centers

The concept of these centers is discussed under Heart and Vascular Diseases.

Prevention, Education, and Control

Sickle Cell Anemia and Cooley's Anemia

Despite the fact that much is known about sickle cell disease and Cooley's anemia, the general public, including actual and potential victims, have a poor understanding of these disorders and their ramifications. The NHLI is developing a program to increase public awareness regarding these diseases.

- The goals of the control program are to educate the public about sickle cell disease and Cooley's anemia and to demonstrate techniques for appropriate screening and counseling.

We need to determine the prevalence and distribution of sickle cell disease and Cooley's anemia in this country, particularly the prevalence of carriers of the trait; provide accurate and up-to-date information on these diseases; initiate and expand appropriate community education, screening, and counseling programs; educate the medical and allied health professions about the problems of these diseases; identify and provide guidance for the management of the resulting psychological, sociological and economic problems; and assist individuals with these disorders to attain their maximum potential in life.

Hemophilia

Public awareness is fundamental to prevention of hemophilia.

- The goal of the prevention effort in hemophilia is to educate the public so that hemophilia carriers and patients may make informed decisions regarding their own lives.

Improved methods are being developed for detecting the carrier of hemophilia and using this information in a program of genetic counseling. The Institute will:

- Develop information, education and genetic counseling services aimed at improving hemophilia therapy and preventing hemophilia.

Thromboembolic Disease

Several high risk factors associated with thromboembolic disease are known. It is now possible to identify persons who may be at increased risk of stroke, pulmonary embolism, and thrombophlebitis and take steps to prevent these maladies. The major program goal is to reduce disability and death from thromboembolic disorders by prevention and control of risk factors.

Blood Resources

Special efforts are needed to encourage more effective and economic utilization of the nation's blood resources. A continuing program must be carried out for professional and public information and education about blood resources and the use of effective blood management systems. This is especially true of blood component therapy.

- The goal of this program is to effect, from dissemination of information and education, improved management of the nation's blood resources.

- Develop a coordinated program of hepatitis epidemiology and control.

Overall Actions and Schedule for Prevention, Education, and Control

There are certain action programs and schedules which are applicable in general to all the disease problem areas and which the Institute will initiate.

Actions. In planning for a more effective National Program in consumer and professional information and education, the Institute will:

- Develop information programs for each of the categorical program areas of the Institute.

- Develop better mechanisms, using all media of communication, to disseminate information on heart, blood vessel, lung and blood diseases and blood resources.
- Establish improved means for direct communication with the public.
- Expand programs to aid health professionals in improving the public's understanding and application of new health knowledge and concepts.
- Establish improved means for communication with the scientific community and the medical profession.

The NHLI information and education programs will be developed with the following populations in mind:

- Young people.
- Adult population in general,
- Individuals who have heart and blood vessel, lung or blood diseases which fall within the mission of the NHLI.
- Individuals who may be especially susceptible to heart, blood vessel or lung diseases.
- Health professionals.

The enhanced public education program will stress certain general concepts regarding these disease problems:

- Heart and blood vessel diseases include many different diseases of the heart and circulation.
- Some heart and lung diseases are preventable; for example, rheumatic heart disease following acute communicable streptococcal infection.
- Early prevention, starting in youth, is important.
- Virtually all types of heart and blood vessel, lung and blood diseases can be handled best if diagnosed early and treated properly.
- More patients with heart and blood vessel, lung and blood diseases can be significantly improved by proper treatment, management and rehabilitation.
- Heart, blood vessel, lung and blood diseases do not necessarily prevent one from living comfortably and earning a living, providing the type of work is selected according to the limitations of the individuals.

Schedule. The Institute's current programs in Prevention, Control, and Education are modest. The NHLI proposes to place considerable emphasis on information and education programs during the next five years.

Intramural Laboratory and Clinical Research

	1974 Estimate		1975 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits........	345	$6,787,000	345	$7,298,000	---	+$511,000
Other expenses........	---	14,845,000	---	15,147,000	---	302,000
Total......	345	21,632,000	345	22,445,000	---	+813,000

*Excludes 1973 appropriation restorations

Objectives, 1975

There will be increased support of research in molecular diseases, pulmonary diseases, experimental therapeutics, molecular hemotology, pathology, and veterinary research in 1975.

Purpose

This is a research program within the facilities of the NIH at Bethesda. Within the framework of seeking fundamental knowledge of disease processes, basic studies comprise a significant portion of the program. Such studies range from study of the subtle biochemical mechanisms controlling the central and autonomic nervous systems to a study of the basic functioning of the primitive cell. The balance and major portion of research is directed specifically toward a solution to the various forms of cardiovascular distress. Because of the recognized excellence of its programs, the Institute also attracts many trainees, who, after accelerated and intensive training, return far better equipped for service in the medical and scientific communities.

The Institute has 345 positions for this activity, of which about half are for scientists and physicians and the remainder for technical personnel. Basic and clinical research was carried on in 13 major laboratories and branches through 309 projects in 1973. One hundred hospital beds are at the disposal of the clinical program. Support is given also to a vigorous out-patient clinical program with approximately 5,000 patient visits annually.

Accomplishments and Objectives 1973/1974

The Institute has long been recognized for the excellence and productivity of its Intramural laboratories. Until last year the institute had not engaged in pulmonary research. There is now being formed the nucleus of a research group to explore the biochemical and molecular aspects of lung functions, an area that due to development of new techniques and findings is now open to investigation. In the coming year a clinical service to compliment expanded laboratory investigations will be instituted.

Research continues on the definition of the complex processes involved in the synthesis, transport, and metabolism of cholesterol and other fats.

An intramural intervention trial is well underway testing the effect of treatment of Type II hyperlipoproteinemia on the progress of coronary artery disease. This is a study of individuals who have demonstrable Type II hyperlipoproteinemia. Over 7,000 persons have been screened, out of which over 700 with Type II hyperlipoproteinemia have been looked at in detail in terms of as high as 20 different risk factors of the disease, providing the largest sample studied of this disease to date. Data from this aspect of the investigation is now in process of being prepared for the public. Out of the 700 patients, 60 have been selected and agreed to undergo the more detailed, long term study of the effects of diet and the drug cholestyramine. It is anticipated that unless definitive answers present themselves earlier, by 1976 200 more patients will be added to this study. Increased support for this valuable study is requested.

Other projects include studies in human disease states as well as in animal model systems concerning the mechanism of hemoglobin biosynthesis and the regulatory controls involved in hemoglobin gene expression. The objective is to understand the molecular basis of hereditary anemias, including the thalassemias (Cooley's anemia, Sickle Cell Anemia) in order to be able to devise effective methods for treating these diseases. Since the initiation of this important project less than 4 years ago rapid strides have been made toward an understanding of the underlying causes of these blood diseases. Specifically this small but highly productive research group have for the first time a) developed a cell-free system for the synthesis of a complete hemoglobin molecule; b) isolated human messenger RNA for normal and abnormal human hemoglobin; c) developed a cell-free system capable of synthesizing hemoglobin messenger RNA from human bone marrow chromosomes; and d) established an active clinical service for diagnosis, treatment, and investigation of red blood cell diseases.

This is a truly remarkable record for a new program. In the coming year it will be necessary to expand the clinical and laboratory efforts.

Basic studies to determine what actually occurs in the blood vessel in order to draw a road map of the events continue to provide the foundation for understanding the mechanisms of atherosclerosis. Perhaps the most exciting development in this program in the past year has been the successful development of an organ support system that will permit investigators to monitor the various chemical, thermal, and physical events occurring along the living blood vessel. This provides a kind of break through that permits the investigator to be on the scene of what is indeed happening to result in atherosclerotic deposits which lead to coronary heart disease. Increased support is requested for this program.

Research Management and Program Services

	1974 Estimate		1975 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and bnenfits........	318	$6,264,000	318	$6,736,000	---	+$472,000
Other expenses........	---	9,322,000	---	10,252,000	---	+930,000
Total......	318	15,586,000	318	16,988,000	---	+1,402,000

*Excludes 1973 appropriation restorations

Objectives, 1975

The Institute has assumed a number of new activities in accordance with recent legislation, such as the annual updating of the five-year plan for the National Program, annual reports by the Director and the Council, management of the Interagency Technical Committee, initiation of education and control programs and development of National Research and Demonstration Centers. Implementation of the National Program designed to carry out these new activities will require the Institute staff to assume greater responsibilities for analysis and evaluation of programs and coordination of the national effort.

All of the scientific program divisions of the Institute will be mounting new programs that will require more effective coordination and evaluation. For example, Specialized Centers of Research are planned in several areas, including centers for heart and lung diseases of children; work in the area of lung diseases, now in its early stages, is expanding substantially in several directions; the new National Research and Demonstration Centers will require special staff; the development of non-invasive techniques for diagnosis and monitoring, stressed by each of the advisory panels in the development of the National Plan and by the National Heart and Lung Advisory Council, will require special knowledge of several areas; the Division of Extramural Affairs will provide new and needed expertise in reviewing applications and proposals in areas entirely new to the Institute, such as the National Research and Demonstration Centers and the control programs. The demands of new initiatives and the expansion of current programs will require expertise that is not now available within the Institute.

Purpose

This activity provides support for the Institute Director and his immediate staff (including the Office of Prevention, Control, and Education, the Office of Administrative Management, and the Office of Program Planning and Evaluation) and for professional direction and administration of the Institute's grant and contract programs. All of the staff of the Institute, with the exception of its intramural laboratory and clinical scientists and technical staff, are funded from this activity.

Funds support the overall direction, coordination, planning, administration, and information activities of the varied programs of the Institute. The Director and his immediate staff are responsible for introducing new knowledge into current operating programs and for planning, development, and review of new areas of focus and interest. Funds also provide for scientific and administrative direction of grants and contract programs.

Accomplishments and Objectives 1973/1974

Continued leadership was provided for a greatly accelerated program throughout the Institute on new research initiatives. The National Heart, Blood Vessel, Lung, and Blood Act of 1972 was enacted to "enlarge the authority of the National Heart and Lung Institute in order to advance the national attack upon heart, blood vessel, lung, and blood diseases." This Act required the development of a National Plan to expand, intensify, and coordinate Institue activities and requires that it be updated annually for transmittal to the President and the Congress. The plan was prepared in 1973 and transmitted to the Congress on July 24, 1973.

The DHEW Secretary announced a nation-wide High Blood Pressure Information and Education Program. The Program is coordinated by the Institute and represents one segment of an expanding effort in this area.

The Act also authorizes a total of thirty National Research and Demonstration Centers. These centers have been the focus of much planning by the Institute and the National Advisory Heart and Lung Council. The Council has been provided an expanded advisory role with concomitant staffing requirements. An Interagency Technical Committee has also been established with representation from some thirteen agencies and Departments. The Committee is chaired by the Director, National Heart and Lung Institute, and requires rather substantial staff support.

Following the announcement of the National Blood Policy by the Secretary in the summer, 1973, the Institute has played a catalytic role in the development of an implementation plan for a safe and efficient system of blood collection and distribution. Staff members have met with various segments of the private blood banking sector, representatives of the concerned federal agencies, and the Secretary's office. These efforts have generated a preliminary joint plan which was submitted to the Secretary on January 31, 1974. While this implementation plan is still in the 'draft' stage, it represents a landmark in American blood banking since it is the first time that the major blood banking organizations have submitted a unified program for improving the nationwide collection and distribution of blood, monitoring the safety of the product, and controlling the cost to the patient. The Institute expects to continue its efforts to see that a satisfactory plan is produced and implemented.

The National Sickle Cell Disease Program was initiated in 1971 subsequent to the President's health message to Congress, in which he identified sickle cell anemia as a high-priority disease target. NHLI is responsible for coordinating the program, which has received additional emphasis by the passage of the National Sickle Cell Anemia Control Act in 1972.

A U.S. - U.S.S.R. health accord has been signed. The cardiovascular program involves six specific projects in a very active exchange with the U.S.S.R. For example, Lipid Research Clinics are being set-up in Moscow and Leningrad so that data can be compared with information obtained from the twelve clinics in the U.S. This has required that a standard protocol be developed, translated into Russian, and pretested in the U.S.S.R. so that all laborabory and clinical findings are strictly comparable.

NATIONAL INSTITUTES OF HEALTH

National Heart and Lung Institute

Program Purpose and Accomplishments

Activity: Heart and Vascular Diseases. (Public Health Service Act, Section 301, Title IV, Part B, and Title XI)

1974			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
---	$166,649,000	$573,700,000 1/	---	$174,217,000

Purpose: This activity plans and directs the Institute's research project grant and contract programs in heart and vascular diseases, encompassing basic research, targeted research, clinical trials, and national cardiovascular centers.

Explanation: Research projects supported range from large-scale clinical trials designed to increase knowledge related to the etiology, diagnosis, and management of lipid disorders associated with premature vascular diseases to research in instrumentation leading to image inhancing techniques and analysis to make it possible to locate microscopic femoral lesions. The Institute's investigator-initiated research proposals are submitted by principal investigators through their university or research institution to the NIH. These research project grants are reviewed by an appropriate NIH study section and priorities of awards are based upon recommendations are further reviewed by the National Heart and Lung Advisory Council. Targeted research programs are funded largely through research contracts. Requests for proposals in specific research areas are published in the Federal Register and copies sent to all medical schools and medical research institutions with known programs in the area of the request. Applications are reviewed by external consultants selected by the Institute and by staff. Contracts are negotiated on the basis of these recommendations.

Accomplishments in 1974: Regular research grant programs are being continued. In addition, 20 Specialized Centers of Research continued attacking the high-priority problems of arteriosclerosis and hypertension. The clinical phase of three major arteriosclerosis intervention trials was expanded through the Multiple Risk Factor Intervention Trial, Lipid Research Clinics, and the Hypertension Detection and Follow-up Program. Other continued contract programs concerned clinical cardiac diseases, biomedical materials and devices, and hypertension education and control.

Objectives for 1975: Of major importance in 1975 is the funding of National Research and Demonstration Centers for Heart and Blood Vessels Research. These centers are envisioned as a national resource attached to a major medical complex dedicated to working in close collaboration with the Institute to further its goals through a multi-disciplined, coordinated, yet flexible, approach to research, education, both public and professional, and demonstration of the applicability of the results of research. This budget will provide the level needed to meet commitments for the non-competing continuation of regular research grants and for competing projects to insure a stable continuation of competing research grants. It would supplement the established Specialized Centers of Research, provide for the new research fellowship program and for new activities in cardiovascular prevention, education, and control, and continue the planned expansion of the clinical phase of the arteriosclerosis clinical trials.

1/ For all NHLI programs

NATIONAL INSTITUTES OF HEALTH

National Heart and Lung Institute

Program Purpose and Accomplishments

Activity: Lung Diseases (Public Health Service Act, Section 301, Title IV, Part B, and Title XI)

1974		1975		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
---	$37,906,000	$573,700,000[1]	---	$45,340,000

Purpose: This activity, conducted by the Division of Lung Diseases, is responsible for overall planning, coordination and evaluation of all extramural activities relative to respiratory diseases. Its professional staff has scientific responsibility for administration of grants, contracts and awards relevant to the Division's program goals.

Explanation: Because the Division's emphasis is on programs that will achieve more effective diagnosis, treatment, and prevention of diseases of the lung, the choice of funding instruments--grants or contracts--is dictated by a combination of investigator interest and the Division's assessment of the best supportive mechanisms for realizing a specific program goal. These funding instruments complement each other, the contract being used primarily to foster studies inadequately represented in the investigator-initiated grant program or studies that require close cooperation among investigators who are at different institutions.

Research programs range from studies concerned with the fundamental mechanisms of lung cell metabolism to the development of instrumentation for ventilatory assist and rehabilitation. The scope of research is large as dictated by the diversity of the disease mechanisms of the lung.

Accomplishments in 1974: Regular research grants are being continued, as well as 17 Specialized Centers of Research. The Division also funds 16 Pulmonary Academic Awards. In addition, approximately 50 new Pulmonary Young Investigator Awards will be made, and 50 research contracts will be awarded, including those which emphasize the environmental diseases of the lung.

Objectives for 1975: The estimate for 1975 provides for two National Research and Demonstration Centers, an additional 50 Pulmonary Young Investigator Awards, continuation of the research grant program at the level needed to meet non-competing commitments and to provide for competing projects to insure a stable continuation of the research grant program. The budget will provide for the new research fellowship program, for supplements to the existing Specialized Centers of Research, for new education and control activities in pulmonary diseases, and for the funding of approximately 55 contracts.

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[1] For all NHLI programs.

NATIONAL INSTITUTES OF HEALTH

National Heart and Lung Institute

Program Purpose and Accomplishments

Activity: Blood Diseases and Resources (Public Health Service Act, Section 301, Title IV, Part B, and Title XI)

1974		1975		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
---	$44,976,000	$573,700,000[1]	---	$50,309,000

Purpose: This segment of the Institute plans and directs the Institute's research grant, contract, and training programs in blood diseases and resources, including sickle cell disease, encompassing basic research, targeted research, clinical trials and demonstrations, technological development, and application of research findings.

Explanation: Investigator-initiated research proposals are submitted by principal investigators through their university or research institution to the National Institutes of Health. These research project grants are reviewed by an appropriate NIH study section and priorities of awards are based upon the nature of the proposed research described in the application. Study section recommendations are further reviewed by the National Heart and Lung Advisory Council. Targeted research programs are funded largely through research contracts. Requests for proposals in specific research areas are published in the Federal Register and copies sent to all medical schools and medical research institutions with known programs in the area of the request. Applications are reviewed by external consultants selected by the Institute and by staff. Contracts are negotiated on the basis of these recommendations.

Accomplishments in 1974: Regular research grant programs are being continued, as well as 5 Specialized Centers of Research. In addition, over 70 contracts are being awarded, with emphasis in development of a nationwide blood system, continuation of sickle cell screening and education, and studies of hemoglobin interaction.

Objectives for 1975: The budget for 1975 provides for the establishment of a National Research and Demonstration Center in Blood Diseases. It would supplement the existing Specialized Centers of Research and provide for one new center. In addition, it would provide for the continuation of the regular grant program at the level necessary to meet commitments on non-competing continuations and an adequate number of competing grants to maintain program stability.

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[1] For all NHLI Programs.

NATIONAL INSTITUTES OF HEALTH

National Heart and Lung Institute

Program Purpose and Accomplishments

Activity: Intramural Laboratory and Clinical Research. (Public Health Service Act, Section 301, Title IV, Part B, and Title XI)

1974		1975		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
345	$21,632,000	$573,700,000[1]	345	$22,445,000

Purpose: This is a research program within the facilities of the NIH at Bethesda. Within the framework of seeking fundamental knowledge of disease processes, basic studies comprise a significant portion of the program. Such studies range from study of the subtle biochemical mechanisms controlling the central and autonomic nervous systems to a study of the basic functioning of the primitive cell. The balance and major portion of research is directed specifically toward a solution to the various forms of cardiovascular and pulmonary diseases.

Explanation: The Institute has 345 positions for this activity, of which about half are for scientists and physicians and the remainder for technical personnel. Basic and clinical research is carried on in 13 major laboratories and branches through 309 projects in 1973. One hundred hospital beds are at the disposal of the clinical program. Support is given also to a vigorous out-patient clinical program with approximately 5,000 patient visits annually. Because of the recognized excellence of its programs, the Institute also attracts many trainees, who, after accelerated and intensive training, return far better equipped for service in the medical and scientific communities.

Accomplishments in 1974: A pulmonary laboratory is being established. Work continues on an intervention trial aimed at determining the effect of treatment of Type II hyperlipoproteinemia on the progress of coronary artery disease. Projects continuing are concerned with defining the complex processes involved in the synthesis, transport, and metabolism of cholesterol and other fats, as well as projects on the mechanism of hemoglobin biosynthesis and hemoglobin genetics which will lead to understanding the molecular basis of the hereditary anemias (including Sickle Cell and Cooley's Anemias).

Objectives for 1975: In 1975 there will be increased support of research in molecular diseases, pulmonary diseases, experimental therapeutics, molecular hematology, pathology, and veterinary research.

1/ For all NHLI programs.

NATIONAL INSTITUTES OF HEALTH

National Heart and Lung Institute

Program Purpose and Accomplishments

Activity: Research Management and Program Services. (Public Health Service Act, Section 301, Title IV, Part B, and Title XI)

1974		1975		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
318	$15,586,000	$573,700,000[1]	318	$16,988,000

Purpose: This activity provides the support necessary for the overall managment of the Institute. Included within this activity are: the Director and his immediate staff (including the Office of Prevention, Control, and Education, the Office of Administrative Management, and the Office of Program Planning and Evaluation), and the staffs of the program divisions and the Division of Extramural Affairs, who provide the professional direction and administration of the Institute's grant and contract programs.

Explanation: Funding for this area provides for salaries and other operating costs for the overall direction, coordination, planning, and administration activities of the Institute. All of the Institute staff, with the exception of the Intramural laboratory scientists and technical staff, are funded from this activity.

Accomplishments in 1974: In 1974 continued leadership was provided for an accelerated National Program authorized in the National Heart, Blood Vessel, Lung and Blood Act of 1972. The National Plan required by the Act was transmitted to the Congress on July 24, 1973. The purpose of the plan was to "expand, intensify, and coordinate the activities of the Institute respecting heart, blood vessel, lung and blood diseases....." The Institute has developed the concepts for the National Research and Demonstration Centers which were called for in the Act. In addition, 1974 has seen the implementation of a US-USSR health accord. The cardiovascular program involves six specific projects in an active exchange with the USSR.

Objectives for 1975: In 1975 the Institute will concentrate on continuing to carry out the mandates of recent legislation. New, required activities include the annual updating of the five-year plan for the National Program, annual reports by the Director and the Council, management of the Interagency Technical Committee, initiation of education and control programs, and establishment of the National Research and Demonstration Centers.

[1] For all NHLI programs.

WEDNESDAY, MARCH 27, 1974.

NATIONAL INSTITUTE OF DENTAL RESEARCH

WITNESSES

DR. SEYMOUR J. KRESHOVER, DIRECTOR
DR. ROBERT S. STONE, DIRECTOR, NATIONAL INSTITUTES OF HEALTH
DR. DeWITT STETTEN, JR., DEPUTY DIRECTOR FOR SCIENCE, NATIONAL INSTITUTES OF HEALTH
JOHN P. PATTERSON, EXECUTIVE OFFICER, NATIONAL INSTITUTE OF DENTAL RESEARCH
MRS. FRANCES H. PETTINATO, FINANCIAL MANAGER, NATIONAL INSTITUTE OF DENTAL RESEARCH
LEON M. SCHWARTZ, ASSOCIATE DIRECTOR FOR ADMINISTRATION, NATIONAL INSTITUTES OF HEALTH
LELAND B. MAY, ACTING DIRECTOR OF FINANCIAL MANAGEMENT, NATIONAL INSTITUTES OF HEALTH
CHARLES MILLER, DEPUTY ASSISTANT SECRETARY, BUDGET

Object Classification (in thousands of dollars)

Identification code 09-25-0873-0-1-651	1973 actual	1974 est.	1975 est.
Direct obligations:			
Personnel compensation:			
11.1 Permanent positions	4,794	5,078	5,270
11.3 Positions other than permanent	304	324	329
11.5 Other personnel compensation	47	54	55
Total personnel compensation	5,145	5,456	5,654
12.1 Personnel benefits: Civilian	769	809	841
21.0 Travel and transportation of persons	224	255	258
22.0 Transportation of things	37	56	56
23.0 Rent, communications, and utilities	156	192	210
24.0 Printing and reproduction	76	81	81
25.0 Other services	7,948	8,246	9,008
26.0 Supplies and materials	683	870	876
31.0 Equipment	190	465	465
41.0 Grants, subsidies, and contributions	25,640	33,656	26,513
Subtotal	40,867	50,086	43,962
95.0 Quarters and subsistence charges	−3	−3	−3
Total direct obligations	40,864	50,083	43,959
Reimbursable obligations:			
21.0 Travel and transportation of persons	1	6	6
99.0 Total obligations	40,865	50,089	43,965

Personnel Summary

Total number of equivalent positions	291	269	268
Full-time equivalent of other positions	35	38	38
Average paid employment	323	312	311
Average GS grade	8.5	8.6	8.6
Average GS salary	$14,260	$15,138	$15,473
Average salary of ungraded positions	$11,138	$12,018	$12,253

Program and Financing (in thousands of dollars)

	Identification code 09-25-0873-0-1-651	1973 actual	1974 est.	1975 est.
	Program by activities:			
	Direct program:			
	1. Caries	9,223	10,096	8,995
	2. Periodontal and soft tissue diseases	7,847	10,048	7,281
	3. Restorative materials	3,767	3,382	2,767
	4. Craniofacial anomalies	5,569	8,265	6,099
	5. Pain control and behavioral studies	740	1,127	966
	6. Dental research institutes	6,706	6,850	7,200
	7. Intramural laboratory and clinical research	6,970	7,312	7,596
	8. Research management and program services	3,013	3,003	3,055
	Total, direct program	43,835	50,083	43,959
	Reimbursable program:			
	7. Intramural laboratory and clinical research	1	6	6
	Total program costs, funded [1]	43,836	50,089	43,965
	Change in selected resources (undelivered orders)	−2,971	---------	---------
10	Total obligations	40,865	50,089	43,965
	Financing:			
11	Receipts and reimbursements from: Non-Federal funds	−1	−6	−6
25	Unobligated balance lapsing	6,134	---------	---------
	Unobligated balance restored	---------	−6,134	---------
	Budget authority	**46,998**	**43,949**	**43,959**
	Budget authority:			
40	Appropriation	46,991	45,566	43,959
	Withheld from obligation and expenditure (Public Law 93-192)	---------	−1,607	---------
41	Transferred to other accounts	---------	−10	---------
42	Transferred from other accounts	7	---------	---------
43	**Appropriation (adjusted)**	**46,998**	**43,949**	**43,959**
	Relation of obligations to outlays:			
71	Obligations incurred, net	40,865	50,083	43,959
72	Obligated balance, start of year	28,950	30,016	32,718
74	Obligated balance, end of year	−30,016	−32,718	−26,630
77	Adjustments in expired accounts	−386	---------	---------
90	Outlays	39,413	47,381	50,047

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[1] Includes capital outlay as follows: 1973, $499 thousand; 1974, $415 thousand 1975, $415 thousand.

Excludes $381 thousand in 1974 and 1975 for activities transferred to (in thousands of dollars):

	1974	*1975*
Research resources	371	371
Departmental management	10	10

Comparable amounts for 1973 ($381 thousand) are included above.

WITNESS INTRODUCTION

Mr. **Flood.** We have the National Institute of Dental Research of the National Institutes of Health. The presentation will be made by Dr. Seymour Kreshover, the Director.

We will insert your biographical sketch, Doctor.

[The biographical sketch follows:]

Biographical Sketch

Name: Seymour J. Kreshover.
Position: Director, National Institute of Dental Research, National Institutes of Health, Assistant Surgeon General, Public Health Service.
Birthplace and date: New York, N.Y., June 22, 1912.
Education:
- B.A., New York University, 1934.
- DDS, University of Pennsylvania, 1938
- Ph D, Yale University, 1942
- M.D., New York University, 1949.

Experience:
- Director, National Institute of Dental Research, National Institutes of Health, 1966—present.
- Scientific Director, National Institute of Dental Research, National Institutes of Health, 1956–66.
- Associate Trustee, Board of Medical Education and Research, University of Pennsylvania, 1956–60.
- Professor of Oral Pathology, Director of Dental Research, Director of Graduate and Postgraduate Studies, the Medical College of Virginia, 1949–56.
- Teaching Fellow in Histoanatomy, New York University, 1946–48.
- Military Service—U.S. Army Dental Corps, Chief of Dental Service, 39th General Hospital, 1942–46.
- Calhoun Scholar, Yale University Graduate School of Medicine, 1941–42.
- Carnegie Fellow, Yale University Graduate School of Medicine, 1939–41.
- University Fellow, University of Illinois Graduate School, 1938–39.

Association memberships:
- American Dental Association.
- American Medical Association.
- American Association for the Advancement of Science—Fellow.
- American Public Health Association—Fellow.
- American Board of Oral Medicine—Diplomate.
- American College of Dentists (regent, 1968–72).
- Federation Dentaire Internationale.
- International Association for Dental Research.

Special awards, citations, or publications:
- D.Sc. (honorary), University of Buffalo, 1961.
- Public Health Service Meritorious Service Medal, 1965.
- D.Sc. (honorary), University of Pennsylvania, 1967.
- D.Sc. (honorary), Boston University, 1969.
- Public Health Service Distinguished Service Medal, 1972.
- D.Odont. (honorary), University of Goteborg, Sweden, 1973.
- Author of some 50 publications.

Mr. **Flood.** Do you have somebody to introduce to us?

Dr. **Kreshover.** I have with me Mrs. Pettinato, our financial manager and Mr. Patterson, our executive officer. They both met you last time.

Mr. **Flood.** You have a prepared statement, Doctor. What do you want to do about that?

Dr. **Kreshover.** I would like to read it, Mr. Chairman, in the event that some comments might prompt questions.

Mr. **Flood.** They will. Go ahead.

OPENING STATEMENT

Dr. **Kreshover.** Mr. Chairman and members of the committee. I appreciate the opportunity to appear before you again this year on behalf of the National Institute of Dental Research.

This past June marked the 25th anniversary of the Institute. At a scientific conference held on that occasion, Dr. John S. Millis, president of the National Fund for Medical Education, predicted that dentistry might well be the first branch of medicine to achieve the goal of disease prevention.

This is the goal toward which the Institute is constantly striving. The need has always outpaced the knowledge available to cope with it. But now we are being further goaded by the prospects of overwhelming demand. Only recently, for example, a large industrial union negotiated a contract that will include prepaid, comprehensive dental care for its employees and their dependents. This program alone will add roughly 350,000 persons to the 18 million now covered by some type of prepaid dental care plan in this country, and it may well trigger similar demands by other segments of society.

The need for prevention is especially critical in dentistry because dental diseases, such as tooth decay and gum disease, are not self-limiting. Unless they are treated, they get worse and worse, often paving the way for other problems.

Mr. **Flood.** What does self-limiting mean?

Dr. **Kreshover.** A lesion affecting most oral tissues, once begun, will continue. It is a chronic infection.

Mr. **Flood.** What is the connotation of self-limiting?

Dr. **Kreshover.** An example would be tuberculosis. It could be arrested.

Mr. **Flood.** You are speaking of the thing, not the person?

Dr. **Kreshover.** Yes.

The continuing influence of research on dental education has contributed to a dramatic change in concept from restorative to preventive dentistry. National Institute of Dental Research's impact is undoubtedly an important factor in the recent finding from the health interview survey that the percentage of people in the United States without teeth is decreasing. In 1957–58, the percentage ranged from 22.4 in the 44–54 age group to 67.3 in the 75 and over group. In 1971 the comparable percentages were 17.3 and 59.8.

DENTAL CARIES

The Institute's national caries program is encompassing a broad area, as various leads yielded by the advancing state of knowledge are pursued. Research on patient attitudes toward dental disease and the acceptance of new agents is a component in several projects and reflects our increasing interest in the delivery of new agents to the public.

Techniques under current study offer promise that a total of 80-percent reduction in tooth decay is achievable with present knowledge. This reduction is dependent on the protective benefit of fluoride—through water fluoridation, a regimen of topical fluoride treatments, or both—and the use of an adhesive plastic to seal the pits and fissures of the chewing surfaces of the teeth.

As part of the continuing evaluation of topical fluoride agents, a dramatic illustration of their effectiveness comes from a recent study of cancer patients after X-ray treatments of the head and neck. Such patients suffer rampant caries because X-rays largely destroy their ability to make saliva. Within 2 to 3 weeks after radiation, dryness of the mouth develops, and the relative numbers of specific microorganisms in the mouth change. In an average of 7 months, 195 new caries lesions were found in 11 patients suffering from xerostomia. Conversely, seven patients treated with a topical fluoride gel developed only two new caries sites after 5½ months. Such patients not only benefit from this treatment but may well provide a model for the study of caries and the evaluation of other control measures in shorter periods of time than is possible in the general population.

In another chemotherapeutic approach, the Institute recently contracted with the Royal Dental College at Aarhus, Denmark, for a clinical trial of chlorhexidine, an agent attracting considerable attention for possible control of caries. The target is the control of plaque, a bacterial film that forms on teeth and gums. In this study, dental and medical students rinsed their mouths daily with a 0.2 percent solution of chlorhexidine for 1 minute. Shifts in plaque organisms, differences in plaque and caries incidence, and possible harmful side effects of daily long-term use of the agent are being carefully monitored. Early results show that the numbers of tooth surfaces covered with plaque and the amount of gum inflammation decreased after treatment. Plaque samples were also found to have a 50-percent reduction in certain bacteria. Chlorhexidine has some disadvantages, such as staining of teeth, but perhaps other similar chemicals will be found that are both effective and pleasant to use.

Mr. FLOOD. This is strictly R. & D. right now.

Dr. KRESHOVER. This particular study is.

I might add that we are also examining the nature of salivary protective systems, the degree to which they keep caries under control, and whether they can be reinforced through therapeutic measures.

In short, all avenues to the prevention of caries—combating the microbial agent, increasing the resistance of the tooth, and modifying the diet—are being explored in an effort to achieve as close to 100-percent protection as possible.

PERIODONTAL DISEASE

Studies of periodontal disease are probing various factors believed to cause this pervasive problem.

Mr. FLOOD. What is periodontal disease?

Dr. KRESHOVER. It is a disease, we believe, that is caused by microorganisms of certain specific types that begins with an infection of the soft tissues; the gingiva that circle the necks of the teeth. You can see visually as you examine the mouth that it then progresses as an inflammatory process to involve the underlying tissues resulting in bone destruction as well as destruction of the soft tissue that attaches the bone to the teeth.

A little later on, for the record if you believe you would want to explore it further, I could cite some of the more important research going on today in some of our intramural activities. It clarifies much about the mechanisms of periodontal disease. I think you would find it most interesting.

A prime research target is the role of the bacterial plaque that accumulates below the gum line, which differs in composition from that associated with caries on the crowns of the teeth. More evidence is accumulating that specific bacterial products in the adherent film called plaque activate the body's immune response and trigger the release of chemicals which are thought to destroy structural elements of the periodontal tissues.

It is now becoming clear that different forms of periodontal disease may be caused by different bacteria. Recent studies of one type, in which there is great bone loss and pocket formation but little inflammation and plaque, indicate that there is a distinctly different group of bacteria associated with it than is identified with the more frequent type. These findings suggest that patients with this more rare but highly destructive form of periodontal disease may have an unusual pattern of susceptibility to certain organisms.

I might add that this form of the disease affects principally young people under the age of 20. Unlike what we anticipated, at least in our earlier investigations, periodontal disease does, in fact, very seriously affect young folks.

New findings indicate that the net loss of connective tissues observed in periodontal disease is probably the result of an imbalance between tissue synthesis and breakdown. Emerging evidence indicates that the inflammatory process offers mechanisms which bring about both of these effects. For example, white blood cells found in inflamed tissues have been shown to produce chemicals which destroy cells, fibers, and bone.

Within the limits of present knowledge, dental scientists are also seeking means of improved diagnosis, treatment, and prevention. An earlier study under an NIDR grant showed elevated levels of prostaglandin, a hormone-like substance, in the gums of patients with periodontal disease. In an extension of this study not under the auspices of the NIDR, it was found that vitamin E can block the action of the prostaglandin, which has the demonstrated effect of increasing blood vessel permeability. Whether locally applying a specific blocking agent could inhibit the bone resorption seen in periodontal disease must await studies of longer duration.

ORAL CANCER

Oral leukoplakia, abnormal whitish patches in the mouth, are of interest because they sometimes become malignant. In view of the long-held relationship of smoking to such precancerous lesions, a research team examined whether cutting down or stopping cigarette smoking would cause these patches to disappear. While a decrease in smoking did not appear to have much effect, cessation had a marked effect after only 3 months.

Studies conducted in India under NIDR support with Public Law 480 funds—that I had occasion last year to discuss with you briefly—have culminated in the publication of a diagnostic guide to medical and dental practitioners for the early detection of oral cancer and precancerous lesions. Published by the Tata Institute of Fundamental Research at Bombay, the brochure demonstrates a wide range of lesions often seen in India, where the risk of oral and pharyngeal cancer is the world's highest.

Mr. Flood. India is quite a place. It is a lot of real estate. Is this parochial? Why is it peculiar to India?

Dr. Kreshover. It is a most unusual thing that we have observed in these Public Law 480 supported studies in India. First, in terms of statistics, Mr. Flood, in our country oral cancer constitutes about 4 percent of all cancers. In India it is 40 percent.

Mr. Flood. Why India? Take a look at India. Bombay. What is peculiar about India?

Dr. Kreshover. There are two things in particular that are peculiar about India and about the population we have been studying. No. 1 is their smoking habits.

Mr. Flood. In Bombay?

Dr. Kreshover. Throughout much of India.

Mr. Flood. Throughout much of India?

Dr. Kreshover. Yes, sir. Throughout much of India there is a very widespread cultural habit of reverse smoking. They don't smoke cigarettes the way we do. They will reverse the cigarette and put the lighted end in the mouth.

Mr. Flood. Tobacco?

Dr. Kreshover. Yes.

Mr. Flood. That is a good trick if you can do it.

Dr. Kreshover. This is the way many people, particularly in the province of Andre Pradesh, smoke. In India it is a widespread habit.

Another thing that is widespread in India is betel nut chewing. In doing that they hold the quid on the side of the mouth and there is considerable irritation of the soft tissues.

I think these alone account for a lot of cancer. There is also vitamin A deficiency which is widespread in India. This leads to changes in the epithelial cells which are oftentimes then predisposed to a precancerous condition.

CRANIOFACIAL ANOMALIES

While habilitation research continues, more attention is now being given to causes of craniofacial malformations so that one day we may be able to reduce their incidence.

One noteworthy result of the past year was the confirmation of a suspected increase in risk of cleft lip and palate among children of epileptic women, believed to be due to the anticonvulsant medications taken by these women. It is Dilantin particularly that I am referring to. Since these medications reduce serum folate levels, the findings suggest an important role of folic acid metabolism in the genesis of oral clefts. It is hoped that future studies, both in animals and humans, will further test this hypothesis.

Another significant finding is that low, single doses of X-radiation markedly increase the frequency of spontaneous cleft lip and palate in certain mice that have a genetic predisposition to it. The results also suggest that, at a very precise developmental period in the rodent experiments, radiation will selectively cause resorption of fetuses that are prone to cleft defects. Scientists assume from these findings that relatively minor environmental stresses may allow a genetic defect to appear.

IMPLANTS

As I reported to you last year, we are expanding our research on implants. Good experimental data are sparse, and we need to know much more about the performance of implants before they can be recommended for use by the general public. Recently initiated studies include different animal models to test various materials, techniques of implantation, and implant shapes. Despite statements of long-standing success that have appeared in the public press, implants generally last only up to 2 years, then fail. Obviously, therefore, more extensive basic and clinical research is required.

DENTAL TECHNOLOGY

Institute scientists are investigating ways to minimize the hazards of X-rays without compromising image quality. This involves the identification of basic factors limiting diagnostic performance. As a spinoff of these studies, a new type of radiographic system is being developed, which combines the advantages of instantaneous image production with a significant reduction in the amount of radiation required for diagnostically acceptable results.

DENTAL RESEARCH INSTITUTES

The program of Dental Research Institutes and Centers, authorized 7 years ago, has made possible a new infusion of scientific talent that is giving greater vigor to the total research effort against oral diseases. As the five institutes now in existence under this program mature, they are becoming more mission-oriented. Thus, although the focus of each institute varies, collectively they embrace research efforts covering the broadest spectrum of oral-facial disease.

A deliberate effort is also being made by these centers to encourage greater collaboration with other institutions, regardless of geographic boundaries, and most particularly schools of dentistry.

Another area you queried me on in the past is with regard to communications with practitioners.

COMMUNICATING WITH PRACTITIONERS

One of our continuing concerns is to bring the latest research findings to the attention of the dental practitioner. Our communications efforts extend beyond presentations of research papers before professional audiences and publication in appropriate journals. For example, each month, releases on current research developments are sent to the dental press. Abstracts of studies by NIDR scientists are also published quarterly and made available to those interested. In addition, reports of leading dental scientists on progress against oral-facial diseases and prospects for the future were published this past year. These reports, representing the proceedings of NIDR's anniversary conference, were published as a special supplement to the Journal of the American Dental Association and distributed to the profession.

We also sent your office a copy, I know.

BUDGET REQUEST

In conclusion, Mr. Chairman, the budget request for the National Institute of Dental Research for fiscal year 1975 is $43,959,000. I shall be pleased to try to answer any questions and supply additional information desired for the record.

Mr. Flood. This budget request you are talking about for the National Institute of Dental Research includes an increase of $4,000 over the 1974 adjusted appropriations; right?

Dr. Kreshover. Yes, sir.

IMPOUNDED FUNDS RESTORED

Mr. Flood. In 1974 you received $6,134,000 in restored 1973 funds?

Dr. Kreshover. Yes, sir.

Mr. Flood. How did you spend that money? In what programs did you invest these funds? Did you use any of the 1973 money to fund these multiyear, 2 years or more, grant awards?

Dr. Kreshover. The release of the restored funds out of the 1973 appropriation, Mr. Flood, as we understand it, have been to use restored funds as they would have been used if available in fiscal year 1973. This could include a small number of awards in excess of 12 months which was our normal programing practice.

The spread of how the dollars have been used specifically, we can introduce now for the record, or relate to you.

Mr. Flood. For the record.

[The information follows:]

DISTRIBUTION OF 1973 IMPOUNDED FUNDS

Budget mechanism	Number of awards	Amount (thousands)
Research grants:		
Caries	3	$674
Periodontal and soft tissue diseases	4	541
Restorative materials	2	70
Craniofacial anomalies	7	938
Pain control and behavioral sciences	1	36
Subtotal	17	2,259
Fellowships:		
Caries		51
Periodontal and soft tissue diseases		336
Restorative materials		10
Craniofacial anomalies		262
Pain control and behavioral sciences		20
Subtotal		679
Training grants:		
Caries		110
Periodontal and soft tissue diseases		937
Restorative materials		280
Craniofacial anomalies		841
Pain control and behavioral sciences		73
Subtotal		2,241
Research and development contracts: Caries	2	175
Total	19	5,354

MULTIYEAR GRANT AWARDS

Mr. **Flood**. Did you use any of the 1974 funds to make any of these multiyear grant awards?

Dr. **Kreshover**. Yes, sir, we did some.

Mr. **Flood**. What is the impact of the multiyear grant award on your 1975 budget request?

Dr. **Kreshover**. Approximately $2,500,000, in round figures, will be allocated for use in the next fiscal year, in 1975.

Mr. **Flood**. Take a look at page 137 of your justification. Will you submit for the record a revision of that table on page 137? Specifically, I want to see in the 1974 column the restored funds; and of course, in the 1975 column, the impact of the action you have taken in 1974.

Dr. **Kreshover**. We have that table and can introduce it for the record.

[The information follows:]

NATIONAL INSTITUTE OF DENTAL RESEARCH

Obligations by Budget Mechanism
Showing "True" Program Levels
in 1974 - 1975
(Amounts in thousands)

Budget Mechanism	1972		1973		1974		1975	
	No.	Amount	No.	Amount	No.	Amount	No.	Amount
Grants								
Regular								
Non-competing	142	$8,407	199	$11,506	170	$9,599	185	$12,000
Competing	39	2,857	30	1,679	23	2,632	24	1,146
New	72	2,461	43	1,227	50	2,207	11	500
Supplemental	(11)	112	(5)	254	(6)	220	-	-
Subtotal	253	13,837	272	14,666	243	14,658	220	13,646
Special								
Specialized Research Centers	1	361	1	361	1	342	1	342
Dental Research Institutes	5	6,500	5	6,200	5	6,850	5	7,200
Research Career Program	26	582	22	506	33	764	33	764
Scientific Evaluation	-	-	1	36	1	36	1	36
Subtotal	32	7,443	29	7,103	40	7,992	40	8,342
Total Grants	285	21,280	301	21,769	283	22,650	260	21,988
Fellowships								
Non-competing	30	408	34	426	18	220	195	3,800
Competing	1	7	1	21	4	120	-	-
New	33	307	3	60	140	1,639	40	600
Supplemental	-	-	-	-	(2)	100	-	-
Subtotal	64	785	38	507	162	2,079	235	4,400
Training Grants								
Non-competing	68	4,010	53	2,187	36	3,153	47	3,025
Competing	14	1,067	8	536	7	433	-	-
New	4	159	-	-	-	-	-	-
Supplemental	(4)	34	(18)	306	(24)	1,800	(24)	600
Subtotal	86	5,270	61	3,029	43	5,386	47	3,625

NATIONAL INSTITUTE OF DENTAL RESEARCH

Obligations by Budget Mechanism
Showing "True" Program Levels
in 1974 - 1975

(Amounts in thousands)

Budget Mechanism	1972		1973		1974		1975	
	No.	Amount	No.	Amount	No.	Amount	No.	Amount
Lab & Clinical Research..................		$6,235		$6,432		$7,282		$7,596
R & D Contracts..........................		5,267		4,996		5,083		4,908
Collaborative Research & Support.........		894		959		1,086		1,127
Res. Mgmt & Program Services.............		2,518		2,747		3,003		3,055
TOTAL....................................		42,249*		40,439		46,569		46,699

*GRSG Funds of $1,040,000 not included in FY 1972 for comparable obligations.

NATIONAL INSTITUTE OF DENTAL RESEARCH

Obligations by Budget Activity
Showing "True" Program Levels
in 1974 - 1975
(Amounts in thousands)

Budget Program	1973		1974		1975	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Caries	34	$8,515	34	$9,263	34	$9,844
Periodontal and Soft Tissue Diseases	-	7,240	-	8,667	-	8,076
Restorative Materials	-	3,463	-	2,978	-	3,041
Craniofacial Anomalies	-	5,137	-	7,509	-	6,811
Pain Control	-	705	-	1,017	-	1,076
Dental Research Institutes	-	6,200	-	6,850	-	7,200
Intramural Laboratory and Clinical Research	186	6,432	165	7,282	165	7,596
Research Management and Program Services	71	2,747	69	3,003	69	3,055
Total Obligations	291	40,439	268	46,569	268	46,699

NATIONAL INSTITUTE OF DENTAL RESEARCH

Multi-Year Funding From 1974 Appropriation

Budget Mechanism	No. of Awards	Total Amount	Amount Effecting 1975 Funding	Remarks
RESEARCH GRANTS:				
	2	$1,198	$599	Caries
	2	540	270	Periodontal and Soft Tissue Diseases
	1	106	53	Restorative Materials
	1	106	53	Craniofacial Anomalies
	1	50	25	Pain Control and Behavioral Sciences
Subtotal..................	7	2,000	1,000	
FELLOWSHIPS:				
	4	300	250	Caries
	8	980	365	Periodontal and Soft Tissue Diseases
	3	243	167	Restorative Materials
	39	1,068	659	Craniofacial Anomalies
	1	209	59	Pain Control and Behavioral Sciences
Subtotal..................	55	2,800	1,500	
TRAINING GRANTS:				
	0	0	0	Caries
	2	320	160	Periodontal and Soft Tissue Diseases
	1	108	54	Restorative Materials
	0	0	0	Craniofacial Anomalies
	1	52	26	Pain Control and Behavioral Sciences
Subtotal.................	4	480	240	
RESEARCH AND DEVELOPMENT CONTRACTS	0	0	0	

RESEARCH GRANTS SUPPORTED

Mr. FLOOD. How many new grants will you be able to make in fiscal 1975 with the budget request?

Dr. KRESHOVER. There are two ways of looking at the figures, and you may want to examine both.

In fiscal 1974, our current year, we are projecting new grants, that is types 1 and 2, as numbering 56 in the aggregate amount of some $3.8 million. We project that these monies will be used to support 49 research grants of the regular type, averaging approximately $60,000 per grant, and seven program projects, averaging approximately $211,000 per program project. If we look at the projections for 1975 we will be funding some 33 regular research grants. We probably will not be able to fund any program projects. The 33 regular research grants will be funded at an aggregate level per grant of some $50,000 in contrast to the current funding per regular research grant of $60,000.

FLUORIDATION

Mr. FLOOD. In your justifications you state you have made progress in increasing tooth resistance to caries with new topical fluoride.

Dr. KRESHOVER. Yes.

Mr. FLOOD. Is this going to take the place of the fluoridation of all community water supplies?

Dr. KRESHOVER. No. We firmly believe, Mr. Flood, that anything we do in the way of additional preventives and control measures to eliminate dental caries as a disease entity, so widely spread in our population, is going to have to take off on top of the base of fluoridation. Fluoridation at the present time results in a decrease of caries of some 60 percent. So one way of looking at it, in a simplistic fashion, is that we have licked 60 percent of the problem and the remaining problem is really to do what fluoridation is not able to do in itself.

So topical gels or fluorides is one approach. The sealant is another approach I indicated earlier. We also are moving in the direction of trying to develop antimicrobial agents and antibiotics. We are moving too in the direction of trying to determine the effectiveness of additives to the diet, and we are trying to examine other possible trace elements, in addition to fluoride, that might have some beneficial effects.

Mr. FLOOD. How often does a child have this topical fluoride applied to the teeth?

Dr. KRESHOVER. We have found that topical fluorides applied in the form of a gel, if they are applied every day for approximately 6 minutes every school day can result in a caries reduction of considerable degree.

Mr. FLOOD. As you know, we are interested in this.

Dr. KRESHOVER. I am sorry. Were you referring to the sealant?

Mr. FLOOD. Yes.

Dr. KRESHOVER. The fluoride gel is repeated each day. The sealant is applied one time and hardened with an ultraviolet ray.

Mr. FLOOD. Can this be done by a paramedic?

Dr. KRESHOVER. Yes.

Mr. FLOOD. Is this expensive?

Dr. **Kreshover**. Very inexpensive.

Mr. **Flood**. Can the average family afford this topical fluoride?

Dr. **Kreshover**. Yes, sir.

TOOTH SEALANT

Mr. **Flood**. Last year you told us you were conducting clinical trials of adhesive tooth sealant to protect the vulnerable pits and fissures in children's teeth.

Dr. **Kreshover**. Yes.

Mr. **Flood**. Have you completed your studies on this? Are you ready to go to town with this item?

I asked this because the HMO bill that just became law says an HMO must, in addition to all of the other benefits, provide its members with topical fluoride application. We want to be sure that the state of the art is such that HMO's can deliver the service. What about it?

Dr. **Kreshover**. Topical fluorides have been in use for a number of years and their benefits are well known. But with regard to topical sealants, although they are already on the market and are being used to some extent in dental practice, it is the position of our Institute that all of the answers are not yet in. We, for example, have just now completed 2 years of a projected 3-year study in a small community in Montana. The results of this study would indicate there is a reduction in dental caries after 2 years following a topical sealant application in the range of some 67 percent. The earlier findings, you may recall, Mr. Flood, were ranging in the area of over 95 percent reduction in dental caries.

We don't know, for example, whether a sealant that has been used during the childhood years and then is discontinued after that would have any long-range effect in altering or preventing the final maturation of the biting surface of the tooth. So we are cautious at the moment. We recognize the fact that sealants do work, they are highly effective, they are safe. But on the other hand, we would like to reserve a final judgment in our Institute before advocating their widespread public use.

PERIODONTAL GUM DISEASES

Mr. **Flood**. You were talking about periodontal gum diseases. You told us last year over 20 million Americans have lost all of their teeth as a result of periodontal disease. This year in your justification you say——

Dr. **Kreshover**. 22.6 million.

Mr. **Flood** (continuing). Treatment of this disease is time-consuming, costly, frequently unsuccessful, and remains essentially unavailable to the majority of the population because of the high cost and shortage of periodontists.

What are you doing about this problem? How will this kind of budget help you do it?

Dr. **Kreshover**. The state of the art and our understanding of periodontal disease is not nearly as advanced as it is in dental caries, and accordingly, we don't have what we have identified in the national caries program as a kind of R. & D. operation. We believe that in the area of periodontal disease, extension of basic research, very fundamental research, must be continued.

I would like to call your attention on this occasion to some very significant developments in terms of our understanding of the mechanisms of periodontal disease that have emanated largely from our intramural operation in the Institute.

In our laboratory of microbiology and immunology, we are beginning now to look at the immunopathology of the lesion of periodontal disease. We are no longer looking only at the effect of the bacteria on the tissues, but rather we are looking at the response of the host from the standpoint of complex immune systems to the presence of the microorganisms.

Some very significant findings have emerged as a consequence of our intramural efforts in this regard. We know, for example, that there are now two types of immune responses that relate to periodontal disease, both implying an effort on the part of the host to protect itself from infection; but in the protecting process, causing damage in terms of inflammatory response that results ultimately in the loss of tissues, in the loss of teeth.

TOOTH IMPLANTS

Mr. **Flood**. Now on the implants, in your general statement you say "despite statements of long-standing success that have appeared in the public press, implants generally last only up to 2 years, then fail. Obviously, therefore, more extensive basic and clinical research is required."

What are you doing in this budget to encourage more extensive research in tooth implants?

Dr. **Kreshover**. This is one of some long standing. We do not as an Institute like the rather widespread practice in dental offices where implants are being used.

It is our position, based on the meager research findings to date, that this is very premature indeed. As a matter of fact, we have worked very closely with the American Dental Association's Council on materials and devices, and they, as a consequence of these deliberations and a symposium that we jointly sponsored, have come out with very straightforward comments, publicly stated, that we cannot yet understand, on scientific grounds, why some implants succeed and why others fail. We cannot yet make a statement of any value whatever with regard to the kind of training required either by a professional or a paraprofessional in order to contribute to the implant technique in dental offices.

Finally, of course, we deplore as an Institute, as does the ADA, any practice whereby in short courses, lecture and otherwise, or brief continuing education experiences, people will presume to become experts in implant technology for use in dental offices.

Mr. **Flood**. In addition to this existing research you are talking about, could we do more research in tooth implants?

Dr. **Kreshover**. We are limiting our research at the present time to experimental animals in model systems, primarily to the baboon which is a very valuable animal to use in experimental designs.

We, for example, made some significant contributions partly contributed by intramural staff.

As you well would recognize, several kinds of materials could be used for implants synthetically prepared. We could use metals, ceramic materials, plastic materials. At the present time we believe that the best material, at least in experimental trial, is calcium aluminate. That is a ceramic material which can be processed to the extent where even its bore size can actually be controlled. We find when an implant is placed in a tooth socket that there is development of new fibrous tissue and new bone. If the porosity of the implant is such that it would encourage the movement of these fibrous tissues and bone into the implanted root, you obviously will enhance its retention.

We also know that a calcium aluminate implant is inert. We know it does not have any teratological properties. We know it can be molded into specific shapes.

We know furthermore in the baboon that these implants have been notably successful to the point where they have been rigidly set for a period of up to 2 years.

We believe the time is at hand now for very limited clinical trials to try to determine exactly how and what the conditions are for assuring success.

PRIMATE TESTING FACILITIES

Mr. Flood. On these primate testing facilities, in your justification you state "contracts will be awarded to establish a primate testing facility" and so on. Will this be in conjunction with one of the primate centers now supported by the NIH Division of Research Resources?

Dr. Kreshover. We are currently contracting, Mr. Flood, for the use of subhuman primates with one setting in the Maryland area, and this is going to be primarily to further our studies in the asessment of vaccine approaches to the control of dental caries.

I believe the primate reference I might have made here in my statement had to do with dental caries more so than with the implant field. I can't recall.

Mr. Flood. Don't you have facilities, and why wouldn't it be cheaper if you did use them? You would save a lot of overhead, for example. Why not?

Dr. Kreshover. It is our experience, Mr. Flood, based on some earlier studies that we did in the congenital anomalies field, that contracting, for example, with Hazleton in the local area had a considerable advantage. The breeding and maintenance of the monkey in our own facilities would be extremely impractical because of space limitations, because of the high cost of maintaining the subhuman primates in terms of care.

It is a very complex operation. I do not know too much about it, but I have worked with monkeys in previous years and it is no mean task and no mean physical operation that you have to maintain to accomplish the job satisfactorily.

DENTAL RESEARCH CENTERS

Mr. Flood. On dental research centers, in your general statement you say "Dental research centers mature and are becoming more mission-oriented." What do you mean by that?

Dr. KRESHOVER. We mean the same kinds of things that Dr. Stone was referring to effectively in his opening statement, and that is that we as an Institute, as part of NIH, also have a mission, and our mission is certainly to do something about the problems of oral and dental diseases that afflict the people in this country. Accordingly, when we refer to our efforts as being mission-oriented, I am very concerned that the words "mission-oriented" not connote an applied effort or R. & D. effort. And we believe in our internal operation in the Institute, as well as our grant supported operations, that we are referring to basic research, very fundamental research. Whether the basic research be conducted in the laboratory or in the clinic, it is all conducted in order to underpin our efforts to do something to meet our mission responsibility.

So the National Institute of Dental Research began its "centers" program, as you would recall, by introducing it in university settings, to attempt to attract into dental research people, eminent scientists, capable scientists, who had not heretofore even remotely thought of dental research as an attraction or an interest. I think once these people have been attracted, and the program is 7 years old now, they begin to recognize the critical and very exciting challenges of applying basic research to the mission of the Dental Institute. This is what we mean by that. They are honing down in their basic research on problems relating to caries and periodontal disease and craniofacial anomalies and the like.

Mr. FLOOD. Can you provide a list of the centers?

Dr. KRESHOVER. There are five of them. One is at the University of Alabama.

Mr. FLOOD. For the record a list of the centers and a brief description of the work being done in each one of the centers.

Dr. KRESHOVER. Right.

[The information follows:]

DENTAL RESEARCH INSTITUTES/CENTERS AND BRIEF PROGRAM DESCRIPTIONS

INSTITUTE OF DENTAL RESEARCH, UNIVERSITY OF ALABAMA

The Institute of Dental Research fosters interdisciplinary research in the areas of: (1) mineralization, (2) connective tissues, (3) caries, and (4) periodontal diseases. Fundamental studies in mineralization and connective tissues are geared toward understanding the disease process in caries and periodontal diseases. Caries studies include clinical testing of anticaries agents and the relationship of microbial flora to caries. Studies of periodontal diseases include the relationship of enzyme activities to the clinical status of the tissues.

DENTAL RESEARCH INSTITUTE, UNIVERSITY OF MICHIGAN

The Dental Research Institute focuses interdisciplinary research efforts on three areas: (1) periodontal disease and caries, (2) viral diseases of the oral cavity, and (3) growth and function of the masticatory apparatus. Within these three areas, studies deal with selected problems at levels ranging from the molecular-analytical to the descriptive and experimental clinical.

REGIONAL DENTAL RESEARCH CENTER, UNIVERSITY OF NORTH CAROLINA

The Regional Dental Research Center supports fundamental research related to (1) periodontal and soft tissue diseases, (2) craniofacial anomalies, and (3) restorative materials. It also has a developing program of fundamental and clinical studies related to the control of pain.

CENTER FOR ORAL HEALTH RESEARCH, UNIVERSITY OF PENNSYLVANIA

The Center for Oral Health Research has established interdisciplinary research programs in the following areas: (1) molecular structure of oral tissues, (2) molecular biology of oral bacteria, (3) immunobiology of the oral cavity, (4) periodontal tissues and dental plaque, and (5) replication of herpes simplex virus. It is developing programs to study dental sealants in relation to orthodontic bonding and to study the interaction of oral bacteria with inflammatory cells.

CENTER FOR RESEARCH IN ORAL BIOLOGY, UNIVERSITY OF WASHINGTON

The Center for Research in Oral Biology supports interdisciplinary research in the areas of: (1) periodontal disease, (2) salivary secretions, (3) nutritional effects on oral and para-oral structures, and (4) pain. Both fundamental and clinical studies are conducted with the major emphasis placed on periodontal disease.

PUBLIC COMMUNICATIONS

Mr. Flood. Public communications. How are you making the public and the practicing dentist aware of these benefits of using topical fluoride and some of the other preventive techniques in your Institute? Could you do more if more resources were made available?

Dr. Kreshover. Dr. Stone and others may have already made reference to the focus at NIH of the so-called Office of Scientific and Health Reports. Our Institute, like other institutes, maintains this kind of very critical operation within its setting.

I would refer to a few figures that may be valuable to have in your record.

In the first instance, public inquiries handled by this Office of Scientific and Health Reports in our Institute in the year numbered something over 11,000. A total of close to 78,000 publications were distributed by our Office of Scientific and Health Reports, and these were directed not only to the lay public but also to the practicing dental community. They translated, in simple language, the kind of contributions that the Institute is making, and also many things the lay public as well as the practicing community could apply on their own behalf as well as in their practices.

I could call attention, for example, to a pamphlet that has been produced as part of a series for consumer information, called "Tooth Care," that has been very much in demand.

I would also call attention to the fact that our NIDR staff professionals have now participated in some six radio programs. In addition to that, the Office of Scientific and Health Reports has prepared and produced a sound and color insert for television news broadcasts on the use of topical fluoride applications for schoolchildren in rural Virginia. I saw this a couple of months ago, and it was a superb film. It has been now widely distributed throughout the United States as well as on the international television circuit.

I could cite many other examples of kinds of things that our Office of Scientific and Health Reports does in our Institute and that comparable offices do in other Institutes at NIH that really respond most directly to the intent of your question.

Mr. Flood. Mr. Michel.

Mr. Michel. Thank you, Mr. Chairman.

IMPOUNDED FUNDS

Doctor, on this unobligated balance of $6,134,000 that you have as a result of impounded funds being released—if you read through every one of the justifications of the Institutes and if one didn't know better, one would get the feeling there was a reduction in every item in 1975, when as a matter of fact what is shown is the ballooning up in 1974 of these previously impounded and unobligated balances.

Let me just ask you, in the delay of obligating that kind of money have your priorties changed at all? In other words, if you had been in a position of obligating much earlier, would it have gone for something different than what it will be going for today that they are released?

Dr. Kreshover. I think not, Mr. Michel.

Mr. Michel. It is pretty much the same?

Dr. Kreshover. I would think so, yes.

Mr. Michel. In the main, what would that be for?

Dr. Kreshover. One of the things I would like to call attention to, and it is not an evasive tactic on my part, but rather the fact that we do it in our Institute, as I am sure other Institutes also do, is that we rely very heavily on state-of-the-art surveys, studies, assessments that go continually through the years. Accordingly, our strategies are almost exactly plotted for a course of 1 year or 2 years ahead in terms, at least, of projecting where the best sites are to conduct certain kinds of research activities, whether they be through contract support or grant support, and our priorities are thus rather well established. I think if there are any alterations in terms of available apportionments to do the job, that this in itself hasn't caused a change in the priorities or reordering of the priorities.

Mr. Michel. I can appreciate and understand that. You wouldn't, however, be so set in your ways that if you looked a year or two ahead and said, "I am sure that is the way I am going to go," but in the meantime something else popped up, you would be flexible enough to make changes.

Dr. Kreshover. By all means I would certainly accept that principle.

Mr. Michel. I can't fault you for having a shorter long-range goal. I wanted the assurances you have just given me that you are pliable and openminded enough to change those priorities if conditions would dictate that.

Dr. Kreshover. Most certainly, Mr. Michel.

MULTIYEAR FUNDING

Mr. Miller. While you are on that topic, the point I want to get on the record relates to one the chairman has been asking each of the Institutes having to do with multiyear funding. We will clear it up in the record and provide the tables, but I think we have perhaps given the impression that multiyear funding may cover both the fiscal year 1973 impounded funds and fiscal year 1974 funds.

We are in fact under court order which does not permit us to multiyear fund NIH 1973 funds, and in fact I don't believe we are doing so. So where there is multiyear funding in NIH, it is out of 1974 funds. I don't think we made that clear, and it may give the impression we have been doing what the courts said not to do.

Mr. MICHEL. What happened to the 1973 money?

Mr. MILLER. As I understand it, the 1973 money is being put out in the normal 1-year project grants.

Mr. MICHEL. I see. So the multiyear money would be limited to what was appropriated for 1974?

Mr. MILLER. For 1974, yes. There is an exception at HEW to that, but not as I understand it at NIH.

Mr. MICHEL. When we talk of multiyear, are we talking of a maximum of 2 years, or do we go to 3?

Dr. KRESHOVER. We are thinking in terms of 2 years.

Dr. STONE. There are a few instances in other Institutes where they have special programmatic needs for flexibility but it is my understanding that they are quite unusual.

PREVENTIVE CARE

Mr. MICHEL. Isn't our top priority in dentistry one of prevention?

Dr. KRESHOVER. No question.

Mr. MICHEL. We make the most gains for the dollars there, don't we?

Dr. KRESHOVER. Yes. We recognize the activities that you have personally had with the American Dental Association and others. One of the things I believe, Mr. Michel, that was covered effectively at our 25th anniversary conference emphasized this very point of prevention. We can't get anywhere in our field of activity without emphasizing prevention.

The manpower requirements in terms of dental care across the board, even if we use every possible auxiliary we could command, would never begin to even scratch the surface.

We are moving very positively in the area of prevention and I think making some rather considerable progress, particularly in the area of dental caries; and I think we are now advancing our base of fundamental knowledge with respect to the peridontal diseases.

Mr. MICHEL. Do we have any specific cases we might cite? I won't ask you to do it now but for the record. What preventive measures put into practice have resulted in progress in a given community or age bracket that we might point to?

Dr. KRESHOVER. Would you want this for your own interest or for the record?

Mr. MICHEL. For the record. I think I have convinced myself. My object here is to convince some other people what we think is right, that we have got to place more and more emphasis on prevention in the field of dental care.

Dr. KRESHOVER. At the invitation of an association in dentistry that is concerned with prevention—I can't remember the specific title—we were asked a couple of months ago to prepare this kind of paper for its use and publication of very specific contributions that could be used by the practicing community. Would this serve the purpose of this subcommittee?

Mr. MICHEL. Yes.

[The information follows:]

Preventive Measures

The leading preventive measure in dentistry continues to be water fluoridation. Drinking fluoridated water from birth has been shown to reduce caries up to 60 percent. Only 1 part per million is necessary—equivalent to about one drop in a bathtub half full of water. It costs only 13 cents a year per person to fluoridate a community's water supply.

Cost benefits of water fluoridation are illustrated in the following examples:

In the nonfluoridated area of Kingston, 5 and 6-year-old children averaged twice as many corrective dental services as children in fluoridated Newburgh, with 60 percent greater cost and almost twice the dentist treatment time, according to the New York State Department of Healh.

A similar decline of 50 percent in the number of decayed, missing, and filled teeth has been reported for children in Chicago.

Comparable savings are reported from other sources. For example, in the California communities of San Francisco and Vallejo—both fluoridated—dental costs of Headstart children were two-thirds lower than costs for the same basic care in the nonfluoridated cities of Berkeley and San Joaquin. Headstart programs in fluoridated communities in Ohio reported similar reduced costs.

In 1969, the Indiana State dental director estimated that every $100,000 spent for fluoridation results in $600,000 in cavities prevented (on the basis of $6 per cavity restoration).

In rural areas where there are no central water supplies, fluoridation of the school water system has proved effective. For example, after 12 years of school water fluoridation at 5.0 parts per million (normal is 1 ppm), children in Elk Lake, Pa., had about 40 percent fewer cavities than their counterparts who were examined before the procedure was initiated.

Although they are not considered as substitutes for water fluoridation, topical fluorides contribute significantly to the reduction of tooth decay. The most effective topical fluoride studied to date by the National Institute of Dental Research is a sodium fluoride gel applied in a custom-fitted mouthpiece. Children tested in a low-fluoride area showed an 80-percent reduction in caries. The gel was applied every school day over a 2-year period. It remains to be seen whether the frequency of use could be reduced without limiting its effectiveness.

If taken regularly, fluoride tablets have been shown to reduce caries in children by 20 to 50 percent. Currently, NIDR is studying the combined effect of a fluoride tablet taken daily and a mouthrinse used weekly in the classroom, supplemented by the use of a fluoride dentifrice at home. New and improved topical fluorides, such as the amine fluorides, are also under study.

The use of a plastic sealant, developed and tested under NIDR support, protects the vulnerable chewing surfaces of the teeth. The pilot study showed that this material was retained in more than 90 percent of sites after 2 years, with practically total protection against tooth decay. A current study shows 66-percent effectiveness after 2 years. Although highly promising, this procedure is considered still experimental by NIDR pending assessment of the retentive and caries-protective properties of the sealant for up to 4 years and an evaluation of the time and skill required for its application on a mass basis.

Another study seeks to determine the degree of protection afforded by the combined use of a sealant and a fluoride gel.

In addition to savings from water fluoridation, referred to earlier, a recent report by the college of dentistry at the University of Iowa indicates that residents of that State, who spend $63 million annually for dental care, can save from $13 million to $23 million each year through the regular use of preventive procedures.

On a nationwide scale, the benefits of water fluoridation and other preventive measures used in dentistry are reflected in the findings of a survey conducted by the American Dental Association. The survey showed a decline in the percentage of patients receiving dentures, fillings, and extractions between 1959 and 1969. During the 10-year period, the percentage of patients receiving fillings declined from 20 to 16 percent and extractions dropped from 13 percent to 9.8 percent. During the same period, prophylaxes (professional cleaning of the teeth) increased from 19.9 to 25.5 percent.

Finally, there are benefits accruing from preventive practices that cannot be calculated in monetary terms. These include: maintenance of natural teeth through life; early detection of such conditions as oral cancer, increasing the likelihood of cure; freedom from pain and discomfort of dental disease; and decreasing productive time lost because of problems brought on by dental disease.

Dr. STONE. It might include information about the costs that had not been incurred for dental care as a result of prevention.

Mr. MICHEL. That is most important. You know the old saying of an ounce of prevention is worth a pound of cure, and this can be shown here.

DENTAL SCHOOLS

I think we have graduated 3,000 or 4,000 dentists a year. Has that changed any?

Dr. KRESHOVER. Our dental school enrollment by my last count totaled 19,000. This covered some 55 operating dental schools today, and I think there are four new ones

Mr. MICHEL. How many now?

Dr. KRESHOVER. Fifty-five and there are four new ones that are either opening their doors shortly or perhaps have already opened their doors in the last few months.

Mr. MICHEL. Do all of those 55 have some form of Federal subsidy.

Dr. KRESHOVER. I dare say there isn't a dental school that doesn't today.

Dr. STONE. They have capitation awards and I suppose also research awards.

Dr. MICHEL. Where are these proposed four new ones?

Dr. KRESHOVER. They are all now open as far as I know. There is one in Colorado, one in Stony Brook, N.Y., one in San Antonio, and a new one just started in Mississippi. I think all of these, with the exception of Mississippi, have already admitted classes; some into facilities that are not entirely adequate. But they are beginning to operate.

Mr. MICHEL. I think in your testimony last year you pointed out that by the year 1980 even with some of this new health manpower legislation we were going to fall far short of our goal of having a sufficient number of dentists to meet the demand.

Dr. KESHOVER. No question.

The American Dental Association, you may remember, projected a need by 1980 of, I think, 178,000 dentists. There are about 102,000 now. With current facilities we will probably reach a level of no more than 120,000 dentists by 1980.

DENTAL SPECIALTIES

Mr. MICHEL. Is there a tendency in the field of dentistry today to go more toward specialization?

Dr. KRESHOVER. I think so.

Mr. MICHEL. Is that too much of a danger yet?

Dr. KRESHOVER. I don't know how many friends I would make among my colleagues in dentistry by saying this, but I would like to view dentistry itself as a specialty of medicine, and I think the tendency to oversubspecialize might have some possible unfavorable impact on the consumer, the user of dentistry.

I have a total here, so maybe the picture isn't as bad as I would have implied. I hastily correct it. Of 100,000 practicing dentists, let's make it 90,000 if we exclude those in Federal employment and so on—there are a total of 12,253 specialists. That is not bad. That means the rest are in general practice. That is a better figure than I thought I could come up with.

Mr. MICHEL. Do you have a figure in the breakdown how many are considered to be orthodontists?

Dr. KRESHOVER. 4,697 by count this year.

Mr. MICHEL. You might break that down further for the record if you will in the specialty categories.

[The information follows:]

Dental specialists

Area	*Number*
Oral surgeons	2, 894
Endodonists	648
Orthodontists	4, 697
Pedodontists	1, 361
Periodontists	1, 260
Prosthodontists	1, 122
Oral pathologists	174
Public health dentists	97
Total	12, 253

DENTAL SCHOOL FACULTY

Mr. MICHEL. Are we getting a sufficient number of good, competent teachers in the field of dentistry? In these new schools is it possible to have professors practicing part time and teaching part time or is that not acceptable?

Dr. KRESHOVER. It is quite acceptable. The average dental school today, and this is a guess but it is within the ball park, would have possibly 50 full-time faculty. This would necessarily be augmented by perhaps as many as 100-plus practicing dentists from the community who contribute to the teaching of the dental student.

I don't think we have nearly enough academicians to staff dental schools. I think as new schools come up, and they are sorely needed, there is much too much raiding, if you will, of faculties from one dental school already established to a new dental school. So we have to do something about increasing our manpower resource of academicians.

I think our dental institute has made a very significant contribution to the educational front. For example, since the year of 1958 when we first began our training program in the Institute we have contributed, through training and fellowships, something over 2,000 teacher-investigators. As many as 700 of these are currently operating in dental schools as teachers and researchers.

Mr. MICHEL. Aside from the raiding factor of a new school against an old school, what are the other inhibiting factors? Is there better remuneration in the field of private practice than in the field of teaching?

Dr. KRESHOVER. I guess to look at the rosier side of the picture, when I graduated from dental school there were two boys in my class, myself and another fellow, who sought to make a career in research and teaching. This might have been a general figure across the board. I would believe this might be. Today, probably for each dental school I would wager you might get as many as 10 or 15 per class who will later be pursuing graduate course work leading to academic experiences. So I think the picture has improved significantly. It is still not enough though.

FLUORIDATION

Mr. MICHEL. Do we still have problems in this country with respect to fluoridation of water supplies?

Dr. KRESHOVER. I guess your problems are about the same as mine in this regard, responding to your constituency. Yes, I believe there continue to be difficult problems. We continue to have to educate the public to accept fluoridation.

It is interesting to note that now fluoridation is mandatory in nine States. Last year either you or Mr. Flood asked me a similar question, and there were seven States then. So that picture is improving.

I think, while the figures aren't notably different in the aggregate, fluoridation in this country is still benefiting only some 46 percent of our total population of 211 million. I think the problem hasn't gone away.

ACUPUNCTURE

Mr. MICHEL. Have we made any progress in the past year in evaluating the research in acupuncture so far as dentistry is concerned?

Dr. KRESHOVER. The greatest activity, if I can steal at least part of the answer from Dr. Stone—the greatest activity at the NIH with regard to an interest in acupuncture is accommodated within the National Institute of General Medical Sciences.

On the other hand, we as an Institute, recognizing that dental pain is almost a caricature of all pain in cartoons depicting the agonies of man—there is nothing quite like a toothache—have become very much interested in pain control, as you will remember from my testimony last year.

Just this year in the reorganization of some of our clinical activities in our Institute we established a new program called neurobiology and anesthesiology. Dr. Dubner, a young dentist who we sent away for graduate training a few years ago in neurophysiology, has been making some of the more important contributions to our understanding of the neural mechanisms in pain relating to the tissues that we are particularly interested in.

As a matter of fact the People's Republic of China has just recently invited a delegation from this country of experts knowledgeable about and greatly interested in the broad field of acupuncture to visit hospital facilities in Canton, Shanghai, and Peking. Dr. Dubner has been invited to go along with their group. I think this expresses our Institute's involvement in the field of acupuncture. We take it for real.

DELIVERY OF DENTAL CARE

Mr. MICHEL. Could we say we have made any progress at all in this country in providing the delivery of dental care to low income families?

Dr. KRESHOVER. I am on very tenuous grounds here when I try to respond to this kind of question.

I would suggest, Mr. Michel, that the most informative response to this question can be provided when the Health Resources Administration, with its Division of Dentistry, comes before this subcommittee and is heard.

I would probably not be very accurate in relating what is being done today to serve the community.

Mr. Michel. When the Administration was putting together its health insurance proposal which, as you know now would also include dental care for children up to 12 years of age, were you folks asked for input there or comment?

Dr. Kreshover. Were we asked?

Mr. Michel. Yes. Did you have an opportunity to express yourself? Do you believe it is a good thing?

Dr. Kreshover. We believe it is very good.

Needless to say, we are very pleased that any health insurance package would, in the first instance, recognize the importance of oral and dental disease which this package does recognize and, secondly, the fact that with limited resources, obviously, the mere fact that they are dealing with the child up to the age of 12 or 13 is in itself progress.

Inasmuch as dental caries and dental disease is most notably a childhood disease, I think this in itself is good. We are pleased that it was not excluded.

Mr. Michel. That it was not excluded?

Dr. Kreshover. Yes, sir.

Mr. Michel. Is there reason to believe it might have been excluded?

Dr. Kreshover. No, I think not. I think today, possibly as a consequence of the fact that NIH has an Institute of Dental Research, dentistry is being accepted more and more as a part of our total health problem in this country, and comprehensive health care demands that dental and oral disease be a part of it.

Mr. Michel. From your assessment of the dental profession out in the country, if I were to put the question to just those in the profession, would I get a favorable response to the proposal that we include dental care for children up to 12 in our health insurance proposal?

Dr. Kreshover. I think today you probably would get a favorable response, yes.

Mr. Michel. Then going back to the way I originally phrased the question, to which I did not get an overwhelmingly affirmative response but a bit of hedging, was there some tension between your shop and those responsible for this proposal?

Dr. Kreshover. No, sir. Candidly stating what I firmly believe, I would think not.

HEALTH INSURANCE

Mr. Michel. Is there anything you would like to say here that you could not say someplace else that would be helpful?

Dr. Kreshover. No. I would like to believe that with a recognition of the importance of problems of oral and dental disease and that they are part and parcel of total human ills, comprehensive health care must not exclude the area of dentistry as a specialty of medicine.

If we had our druthers, of course, we would like to ultimately see all of dental care, without a cutoff in terms of age.

Mr. Michel. If you had any argument to make with the proposal, it would be that it had that cutoff date at 12 years of age?

Dr. Kreshover. We would like to think of comprehensive health care including all age groups, in the ideal situation.

Mr. Michel. Would you suppose that the reason it was not more encompassing than that limitation of 12 was the additional cost factor that might be involved?

Dr. Kreshover. My guess is that the exorbitant cost of dental care might very well have caused it to be limited.

Dr. Stone. I might add one other caution, and that is the availability of resources for care. We could easily swamp the system, I would think.

Mr. Michel. And get ourselves in a box as we did with medicare and medicaid, without the facilities to provide services we were telling everybody they were entitled to.

Dr. Stone. We must be cautious.

Dr. Kreshover. He is being far more practical. I was being idealistic. I hope his response would carry more weight than mine.

Mr. Miller. I am not sure whether it is entirely clear that there is another focal point for the development of health policy with respect to dentistry within the health firmament in HEW. There is a Health Resources Administration which is not oriented toward research at all but, rather, toward care, financing, and this kind of thing. I do not know what role they play, either, in the development of the comprehensive health insurance. They are more focused in the nonresearch area.

Dr. Stone. Ideally, there would be a very smooth continuity between the research effort and the applied effort. When Dr. Edwards testified before you earlier, he emphasized to you his intention and his hope to make that a smooth, unbroken continuity so that there will be constant consultation and collaboration, in the development of applied proposals, with those in the research and theoretical area.

What Dr. Kreshover has said to you, if I understand it correctly, is that in this particular instance, perhaps, that coupling was not as ideal as we would have liked. I am not now talking of a matter of contention or of interagency relationships or anything of that sort. It simply did not happen.

Mr. Michel. Thank you.

That is all, Mr. Chairman.

Mr. Flood. Mr. Natcher.

RESTORATIVE MATERIALS

Mr. Natcher. Doctor, as you know, gold on the world market is now at about $172 an ounce and fixed in this country at about $44 an ounce. What are we doing from the standpoint of research insofar as something to take the place of gold? What about composition of fillings and substitutes? Have we reached the point where no longer gold can be used by dentists? It is hard to get. What are you doing along this line?

Dr. Kreshover. Our activity in dental technology is rather substantial. We do not have any in-house activity in that regard, but we are supporting, primarily through contracts and grants, research designed to improve existing materials.

For example, one of the longest used materials that dentists have in their armamentarium is the so-called amalgam alloy. Amalgam is constituted of mercury, silver, and tin. This is what constitutes the alloy.

One of the very difficult things about amalgam restoration, the silver restoration that most of us have had experience with, is that they fail on two counts. No. 1, they become corrosive and, No. 2, they are extremely low in tensile strength.

Through our support of research, it has been determined that something as simple as substituting gold for silver improves the amalgam. This is a little bit of a reverse in terms of the thrust of your question—it does not require much. The amalgam itself, with a very small addition of gold, will remove its tendency to corrosiveness as well as increase its tensile strength. So, in terms of advancing and enhancing the use of amalgams, this is a very significant contribution.

In another area, we know that chromium, cobalt, and nickel, constituted as an alloy, has wide use in dentistry. It has a deficiency, on the other hand, in that it is not very ductile. This is used in the restoration of prosthetic devices.

One of the things that has been done in the preparation of these alloys is to add to them carbides. Carbides do not increase the strength. As a matter of fact, they contribute to the inadequate ductileness of this alloy. It has been determined, again through our supportive research, that if you add small amounts of tantalum to the cobalt-chromium-nickel alloy you will increase its ductile properties.

In addition to this, of course, we are also making advances in the development of resin materials, methacrylates, acrylics, and so on. I think the whole area of plastics and ceramics, as well as other metals, is moving to the fore when, hopefully, we can use less and less gold in dental practice with enhanced and improved dental care.

Mr. NATCHER. Do you believe at this time that we have a substitute for gold as far as dental practice is concerned?

Dr. KRESHOVER. I think any of the currently available materials on the market, given their proper application in terms of the defect that is being corrected, given exact use and preparation from the standpoint of the know-how of the practitioner, can be every bit as effective as gold in certain instances.

Mr. NATCHER. Thank you, Doctor.

Mr. FLOOD. Mr. Robinson.

DENTAL CARIES

Mr. ROBINSON. Doctor, I think it was 2 years ago that you came before us and the flat statement was made that the cause of dental caries had been isolated, and now the challenge was to cure it.

Last year, the statement of course had to be qualified, and I believe it was because of the fact that in the interim period the discovery had been made that root caries and caries of the upper tooth were not the same, and research was proceeding accordingly. Is that correct?

Dr. KRESHOVER. That is correct.

Mr. ROBINSON. How much closer to being able to make the statement that was made a couple of years ago are you than you were last year with regard to root caries, which presents the real problem now, as I gather?

Dr. KRESHOVER. Let me say, at the outset, that root caries is a very significant problem. You will recall our discussing last time that in the age bracket of 50 years, as an example, the average man or woman afflicted with a new cavity would have a 50 percent chance of this being on the root or on the crown of the tooth.

In contrast, in the age bracket of 60 years-plus, the chances of having root caries in contrast to caries on the crown of the tooth is as high as 70 percent.

So, it is extremely common.

In the age group of 20 to 30, root caries is prevalent only to some 13 percent.

As far as cause is concerned, we know the organisms, the bacteria, that are related to root caries are not the same as those related to coronal caries. We know root caries are related to an organism more akin in its appearance and its characteristics to the bacteria associated with periodontal disease.

This is not too surprising, for the simple reason that root caries is in the same area that periodontal disease attacks, under the gingival margin.

Beyond that, I cannot indicate to you any notable progress, except that we recognize the importance of the disease entity and we recognize, second, the fact that it does relate to a specific category of organism and, third, of course, that it may very well relate in some way to periodontal disease but we are not sure how.

ORAL DISEASES

Mr. Robinson. Yesterday, Doctor, we had a great deal of discussion with regard to the use of tobacco because we had the National Heart and Lung Institute here. I find on page 5 of your statement, the statement that "While a decrease in smoking did not appear to have much effect"—you are discussing oral cancer, of course, "cessation had a marked effect after only 3 months."

Would you enlarge on "marked effect after only 3 months"?

Dr. Kreshover. Not clear in this statement is the fact that we are talking not about the effect on oral cancer per se, but, rather, on precancerous lesions, the so-called white patch in the mouth, the well-known leukoplakia which for a long time has been identified as a clinical observation with the use of tobacco.

There is no question whatever that the complete cessation of smoking with the removal of this kind of irritant will in this brief period of time show a dramatic effect on the prevalence or on the appearance of the leukoplakic lesions in the mouth.

The statement is very well documented in terms of clinical observation.

Mr. Robinson. This means, then, that it takes a period of only 3 months in order for the effects of tobacco to completely disappear?

Dr. Kreshover. To show a reduction in the appearance of the leukoplakic lesions in the mouth.

This is not referring to the oral cancer itself. It also should be clearly stated, Mr. Robinson, that the presence of a lesion of leukoplakia does not in itself connote or imply or indicate that this is invariably going to progress to an oral cancer. It may not.

TOOTH IMPLANTS

Mr. Robinson. How do you define a dental implant? What constitutes an implant as compared to other means that are used to replace teeth that have been lost?

Dr. Kreshover. Only three things can replace a tooth that is lost. No. 1, taking an actual tooth and introducing that into the site where a tooth has been lost. The natural tooth can come from two sources. First, from the same individual, in which case you are dealing with a so-called autogenous graft, taking a tooth from one site to another site in the same individual. These have been moderately successful.

There have been clinical trials, for example, where you take a tooth bud of an unerupted third molar and introduce that into a missing site where a first molar, for one reason or another, has been lost. This has been moderately successful, but not to the point where it has been adopted in practice.

Second, the so-called homologous graft, where you take from one individual of the same species and put into another individual of the same species, has been much less successful.

Third, the heterologous graft, where you take from a different species of animal and put in another species, has been unsuccessful—period.

These are all transplants. We have moved away from that, recognizing the fact they are unsuccessful generally. We have now moved into implants.

Implants are where you take a synthetically prepared material, either a metal or ceramic or plastic, you shape it to the desired size, you introduce it into a prepared site, a socket in the bone and soft tissue, and you observe it for ultimate fixation or retention. These are the experiments we are currently involved in.

I replied to this and it is in the record, Mr. Robinson, to save you time, when Mr. Flood asked a similar question.

Mr. Robinson. Did you reply as to whether or not any damage is caused when an implant is rejected? Can such cause a problem in the future?

Dr. Kreshover. The thing that is most staggering in terms of a problem as we deal with implants is that, unlike an implant that would be used anyplace else in the body, whether it be an implant in terms of bone repair following a fracture or some other kind of implant within the body, a dental implant is exposed to a variety of environments. It is the only kind of implant that is exposed to the outside environment as well as to the inside environment.

It is exposed in the mouth. It traverses soft tissue and ultimately it is fixed into hard tissue, into bone. Therefore, the greatest hazard as we face it in implants is infection. They are lost primarily as a consequence of infection, not as a consequence of being rejected as a transplant would be rejected because of a protein factor in the development of antibodies, in the sense of one tissue not being tolerated by the host.

Mr. Robinson. Is such an infection difficult to reduce?

Dr. Kreshover. The result of this kind of infection, of course, is the fact that the implant is lost. It is remarkable that there are so few infections in the mouth, as you know. If you get bitten by another human, there is nothing quite so infective as a human bite. On the other hand, you wonder why you do not infect yourself more often, because you are living with the same organisms that, when transmitted to another individual, can cause infection invariably. It is remarkable that there are as few infections in the mouth tissues as there are.

RURAL DENTAL PROGRAM

Mr. Robinson. You mentioned the rural dental program among children, and the fact that a film with respect to such a program had been produced in Virginia.

Dr. Kreshover. Yes.

Mr. Robinson. I know at least part of this occurs in the district which I represent. How did it happen that Virginia was selected as the site where this film was prepared, and who paid for the film? Was this paid for by NIH?

Dr. Kreshover. We paid for the film, and I cannot answer, Mr. Robinson, the question of why Virginia was identified as the site. I will have to find the answer for you and send it to you.

Mr. Robinson. I was pleased, nevertheless.

DENTAL CARIES

Doctor, on page 139 of the justifications, you discuss the fact that caries results from three factors—bacterial agents, dietary environment, and tooth susceptibility.

What do we know about tooth susceptibility as a hereditary factor? Knowledge of my own children tells me there is a great deal of differentiation in tooth susceptibility among them. Whereas one never has a cavity, another one will have them every time he goes to the dentist, every 6 months.

Dr. Kreshover. We know very little, indeed, about the genetic factors with respect to tooth decay or dental caries. Some of the earlier work was done at the University of Michigan, I believe, where two individuals, Hunt and Hoppert, first developed a strain of rats that was completely immune to dental caries. Exposed to a caries-inducing diet and exposed to the proper kind of cariogenic organism, they were completely resistant.

Indeed, in our own experiments in our own Institute, when Drs. Fitzgerald and Keyes identified in our laboratory for the first time dental caries as a transmissible disease between animals, we then were also able to demonstrate the fact that certain animal species, certain rats, resisted dental caries.

GENETICS

I cannot give you any account or any information with regard to focusing on what kind of genetic linkage this is in terms of the human resistance or susceptibility to dental caries. There was a study conducted by the Navy at Bainbridge, Md., at the Naval Recruiting Station, that examined the incidence or prevalence of this kind of immunity. I believe they found one in 1,000 Navy recruits was completely immune to dental caries. More recent studies have shown this ratio to be rather less.

We know that it exists, but I cannot give you any accounting of why or how.

Mr. Robinson. Is it the intention of NIDR to get into this area of research to any extent? Is there any point in doing so?

Dr. Kreshover. We believe the genetic predisposition to dental caries is so overwhelming in contrast to the inheritance of resistance that we do not see this as an avenue of research exploration, no, sir.

Mr. Robinson. One final question, Doctor, which has to do with your pain control behavioral studies.

As indicated on page 157, they are directed mainly at the safety of nitrous oxide analgesia and such areas as that. I wonder to what extent we are moving in the direction of getting away from the injection of pain-relieving drugs in the dental-care process.

Dr. Kreshover. As you recall, I believe I responded in part to this a year ago or more.

There are two kinds of pain that we are concerned with in dentistry. One is the symptomatic or organic pain that is there because it is there, and you have to do something to eliminate it through analgesic drugs or some other approach.

The other kind of pain, on the other hand, is the one that we perhaps view as more amenable to our own approaches today, and that is the so-called iatrogenic pain, which is the anxiety, the dread, the fear that people have of going to a dental office, and the sense of pain just in anticipation of what will come about as you sit in the dentist's chair. These relate to our involvement today in behavioral studies.

One State of California study not too long ago indicated some 70 percent of people who go to a dentist are in fear at the prospect of what they will be facing. Ten percent have a fear that is intense. They resist going. Twenty percent, according to this study, which included some 700 families, are favored by an attitude of no fear whatsoever.

Accordingly, our approach in terms of dealing with this at the present time relates to anxiety-relieving drugs. A new drug has been developed largely as a consequence, again, of efforts in our own Institute. Diazepam, a drug which is injected intravenously, causes the patient, as he or she then would receive dental treatment, to have absolutely no memory afterwards of the experience, and have little or no fear or dread as he or she approaches the dental chair for treatment.

Mr. Robinson. I should think that drug would have desirable uses in other areas as well. Things happen around here we would like to forget, too.

I do think, to be serious, that the fear of that needle itself is quite a great one. If it could be avoided, a great deal of the anxiety would be eliminated.

That is all, Mr. Chairman.

Mr. Flood. Mr. Patten.

Mr. Patten. Have you said anything about plastics to prevent cavities?

Dr. Kreshover. Yes, sir. That would be in the record before you came in this morning. Your chairman explored that with me.

Mr. Patten. Do not repeat.

Dr. Kreshover. Yes, sir.

Mr. Patten. I have no further questions.

Mr. Flood. Mr. Obey.

ANXIETY-REDUCING DRUGS

Mr. OBEY. Doctor, I confess to having a great malaise about going to the dentist, as I am sure everybody else does on this side of the table. I would much rather go to the doctor any time than to a dentist.

You mentioned the use of this drug which you say wipes out all memory of the visit to the dentist.

Dr. KRESHOVER. It is an anxiety-reducing drug. I can send you literature on it.

Mr. OBEY. Were you serious when you said—maybe I misunderstood you—it wipes out memory of the experience in the dentist's chair?

Dr. KRESHOVER. Yes, sir.

Mr. OBEY. Do you really think that is a good idea?

Dr. KRESHOVER. Not being a behavioral scientist, I cannot comment on that. I would have to refer you to the literature on the subject and ask you to make your own assumptions about the study.

Mr. OBEY. How much research have you done on the use of that drug?

Dr. KRESHOVER. It is not the only anxiety relieving agent that is available. There are many sedatives, hypnotics, and a variety of other agents that are employed in medical and dental practice today.

The point I wished to make, without focusing down on the specific drug, was the fact that there is a very important issue in dealing with dental care of relieving a patient's anxiety in prospect of some kind of dental treatment.

Mr. OBEY. I recognize that. But I frankly get scared by the tremendous efforts, made in our society to prescribe a drug or a pill, or you name it, for every anxiety from now until the cows come home.

I really think that tendency in itself can be as damaging as one's fears. People do not go to a dentist because they are afraid to go. It scares the hell out of me, too. But if you have a drug that goes that far, I just wonder whether that is really a sensible thing to use.

I would like as much literature on that as you can provide.

Dr. KRESHOVER. I would be glad to send you some literature on that.

USE OF X-RAYS

Mr. OBEY. On page 2 of your statement you mention cancer patients suffering from inability to make saliva after being hit with X-rays.

Dr. KRESHOVER. Yes, sir.

Mr. OBEY. I assume you are talking about substantial X-rays in that kind of condition. This probably is not directly in your line, but I also confess to a malaise because every time I go to the dentist, it is suggested I have another X-ray.

What is the general practice in dentistry around the country in terms of the use of X-rays and its frequency? If a person goes to see a dentist every 6 months, is it the usual practice to give him an X-ray?

Dr. KRESHOVER. It may very well be. I think the two important comments that could be made about your question are:

No. 1, the fact that the industry manufacturing X-ray equipment as well as the film for the recording of an X-ray image has been so tremendously advanced. For example, the X-ray equipment itself, by so-called collimation of the X-ray beam, is one where there is no scattering. You get very little, if any, whole body dose of X-ray, as a consequence, of hazard either to the operator or to the patient.

Dental practice, even in the face of improved equipment, with exact collimation of the X-ray beam, further protection is afforded the patient through use of of a rubber apron.

The second significant contribution has been made in the so-called high-speed films that are used today, where an infinitesimal exposure of the film will cause the X-ray to be adequately replicated onto a film with good imagery.

Mr. OBEY. What percentage of the exposure to X-rays an individual encounters in a given year comes from that kind of use of X-ray?

Dr. KRESHOVER. I would be unable to give you a figure. I would think it would be rather small, as compared, for example, with the X-ray exposure in a GI series or gallbladder visualization or other examination. These would be in a completely different league from what we are dealing with in dental practice.

Mr. OBEY. Would you supply for the record what increments we are talking about?

Dr. KRESHOVER. Yes.

[The information follows:]

X-RAY INFORMATION

Dentistry is responsible for almost half of the total number of radiographs produced annually. In spite of the fact that estimated integral absorbed dose per film is probably lower by a factor of one-third or more for dental films, it is evident that dentistry is responsible for a substantial fraction of the total exposure of the population to diagnostic X-rays. Thus, the implications, in terms of patient risk, are most difficult to determine. Nevertheless, the International Commission on Radiation Protection points out that dental exposures account for less than 1 percent of the estimated genetic significant does of the entire population. Similarly, the average percentage contribution to per capita mean bone marrow dose is also relatively low; i.e., 6 percent for a full month (approximately 14 exposures) dental examination. This is equivalent to the same amount of radiation exposure to the gonadal area a patient would receive from background radiation while walking down the street.

PERIODONTAL DISEASE

Mr. OBEY. On page 2, you also state that the percentage of people in the United States without teeth is decreasing in the age group over 75. You say in 1957 to 1958, the percentage without teeth was 67.3.

Dr. KRESHOVER. Now it is 60.

Mr. OBEY. It has now dropped to 59.8.

I am trying to fit this in with the statement in last year's record.

Dr. KRESHOVER. This was put in the record as a consequence of your statement last year, I believe.

Mr. OBEY. That is what I am trying to get at. Last year it was said that 50 percent of the people over age 55 have no teeth. I asked what the figure would have been 10 years ago, and you said the same.

Then Mr. Miller said the reason you do not see this improvement in statistics in 10 years is that "The population where prevention is going to pay off has not grown up yet."

I take it this is a new study which makes last year's record obsolete?

Dr. KRESHOVER. Mr. Obey, last year I was offering my frank assessment without statistics. As a consequence of your probing at that time, we sought to get accurate figures that were recently available in the survey by the National Center for Health Statistics. These represent valid figures today. I will not comment on Mr. Miller's comment.

Mr. OBEY. You say 20 million Americans lose all their teeth because of periodontal disease.

Dr. KRESHOVER. No, sir. Today 22.6 million Americans are estimated to be missing all of their teeth, and it is our assumption that most of these or a great percentage of these would have been as a consequence of periodontal disease.

Mr. OBEY. Looking at page 128 of your justifications, why the reduction of $367,000 for periodontal disease work?

Dr. KRESHOVER. With fewer dollars in that category, we could break out the impact in terms of what we will be able to support.

Mr. OBEY. I know it is not your fault, but in light of that statistic, is it not shortsighted to cut back in this area? How much do Americans spend on dental care every year?

Dr. KRESHOVER. $5.8 billion.

Mr. OBEY. How much do they spend because of periodontal disease? Have you any idea at all?

Dr. KRESHOVER. Probably in the range of about $1.5 billion.

Mr. OBEY. How much do the 20 million Americans spend for the replacement of their teeth?

Dr. KRESHOVER. I will have to supply that for the record, Mr. Obey. I do not have that figure.

Mr. OBEY. It would be a very substantial amount?

Dr. KRESHOVER. It probably would be, yes, sir.

[The information follows:]

COST OF DENTURES

Based on an approximate average cost of some $400 for a full upper and lower denture, an estimate of cost to rehabilitate 22.6 million edentulous adults in this country would be $9 million. No estimate is available of the number of persons who do not already have artificial dentures.

BUDGET REQUEST

Mr. OBEY. How much did you request for the NIDR?

Dr. KRESHOVER. I have the figure here.

$42,811,000. That was based on the President's budget for 1973, you recall, Mr. Obey, of $38 million-plus, about a $4.5 million increase.

Mr. OBEY. You are asking for $42 million, and the final figure given you was how much?

Dr. KRESHOVER. $43,959,000.

Mr. OBEY. I do not understand. You were given more than you asked for?

Dr. KRESHOVER. The OMB figure was $42.811,000. The figure that is in our appropriation for 1975, the President's budget, is $43,959,000.

Mr. Patterson, can you clarify that point? May I ask him to comment?

Mr. PATTERSON. I believe the $42,811,000 was predicated on the President's budget figure of $38,482,000, and represents an increase of $4.5 million.

Following that, there were other increases presented, so the increase is compiled based on the amount of funds during the course of the budget cycle.

Mr. MILLER. Our first request was made before the compromise was reached and before the 1973 funds were released. So the earlier requests and the first OMB allowance were lower than the final budget.

I think we need to give you something to clarify this and try to make it comparable.

Dr. KRESHOVER. To respond to your first question, Mr. Patterson has provided me with information that I think is explanatory in part.

As a consequence of the increase in terms of mandatory requirements of the Institute, we have necessarily had to make some parallel adjustments with regard to program entities. The mandatory increases were corresponded to by this program adjustment in terms of the specifics of the periodontal disease allocation.

Mr. OBEY. If you look through the reductions here and compare them to the increases in other areas, why would we have such a large decrease in money for periodontal disease research if this is the main reason for total tooth loss in the country?

Dr. KRESHOVER. What Mr. Patterson is saying to me is that much of the adjustment is related to the need for competing versus noncompeting categories in the grants area, the fixed amounts of dollars, for example, that are allocated to continue with the noncompeting requirements of the Institute, with accordingly less available in terms of meeting the competing requirements.

Apart from this, I would also like to interject in terms of response that we have got to look at what we are doing as an Institute as a single instrument of support for research. Accordingly, with the very significant contributions that we are able to make intramurally in our direct operation and the high degree of significant contribution being made in our Laboratory of Microbiology and Immunology specifically relating to periodontal diseases, we believe we probably can get a lot for our money in that kind of enterprise and perhaps with some tradeoffs——

PERIODONTAL DISEASE

Mr. OBEY. In the money you are spending on periodontal versus caries, what has the percentage change been, say, since 1970? What has the percentage change been in each of those categories?

Dr. KRESHOVER. I think it has been significantly increased, quite obviously, in the caries program, and probably in the case of the periodontal diseases a very modest decrease or a plateauing.

Most of our money, you recall, is a consequence of the initiation of the national caries program, and has gone to support that activity. It is the one we were uniquely ready to do a big job in, and accordingly, I think some other things were put in, not a holding pattern, but, rather——

Mr. OBEY. What would you project for the next 5 years?

Dr. KRESHOVER. In terms of what?

Mr. OBEY. That same figure. Assuming you have increases over the next 5 years in both programs, would a larger percentage of the increase go to periodontal?

Dr. KRESHOVER. I think an increasing proportion would necessarily go into the periodontal disease research area.

Mr. OBEY. It seems to me it is your biggest problem.

Dr. KRESHOVER. Yes, sir. There is no question about that.

Mr. OBEY. That is all, Mr. Chairman.

ORAL CANCER

Mr. Conte. How much of your research effort, if any, is related to oral cancer?

Dr. Kreshover. Approximately $500,000, which is spread across programs supported by both research grants and our Institute's intramural activity.

Mr. Conte. How do you coordinate your work with the Cancer Institute?

Dr. Kreshover. This is accomplished by rather well agreed upon collaborations; both extramural and intramural. For example, our Laboratory of Oral Medicine, established about 2 years ago, is pursuing original and very important research in the viral causes of soft tissue lesions of the mouth, notably herpetic infections. As you, of course, already know, Mr. Conte, the Cancer Institute is similarly involved, although in a far greater dimension of support, in searching out the viral aspects of cancer whereas our own efforts, by comparison, are small indeed.

Nevertheless, one of our staff, Dr. Notkins, who is chief of the laboratory I referred to, is a leading figure in virus research and is doing much to clarify the mechanisms of herpes simplex virus infection, its possible relationship to cancer, and the manner in which the viral agent protects itself from the host's defenses. In these activities, close collaboration is pursued with colleagues in the NCI.

With respect to our extramural role in oral cancer research, one of our program areas, concerned with soft tissue diseases, is working in parallel with the Cancer Institute to generate appropriate dental investigations in selected cancer research centers. Examples of such possible sites are the M. D. Anderson Hospital in Texas, and Roswell Park Memorial Hospital in Buffalo.

X-RAYS

Mr. Conte. Do you have any estimate of the actual use of X-rays in the practice of dentistry?

Dr. Kreshover. According to the American Dental Association, in 1969, the last year for which complete data are available, approximately 90 million people visited the dentist. During the same year, dentists made a total of 268,400,000 individual X-ray film exposures. This is an average of slightly under three X-ray exposures per dental patient per year.

I might add that, when modern radiation hygiene techniques are used, the amount of radiation from dental X-rays which reaches the more sensitive cells of the body is approximately the same as that received from natural sources, such as cosmic rays from outer space and radioactive sand and stones, in a single day.

Mr. Conte. Do you have any professional educational efforts on the risks involved?

Dr. Kreshover. It is my understanding, Mr. Conte, that the Food and Drug Administration is emphasizing educational approaches to dental X-ray exposure improvement to supplement its implementation of the new radiation safety performance standards for diagnostic X-ray equipment. However, at the present time, the Federal Government has no authority to regulate X-ray user practices.

RESEARCH GRANTS

Mr. Conte. You're only estimating the award of 11 new research grants this year. That sounds like a phaseout of the research grant program for the Institute. Is it?

Dr. Kreshover. It is correct, Mr. Conte, that we are projecting the support of but 11 research grants in fiscal year 1975 at an average level of $45,500 each. However, this in no way represents a phaseout. For this same year, we are projecting the award of some 178 research grants in the noncompeting category at an aggregate level of some $11 million, and a parallel award of approximately 24 regular research grants supported at a level of almost $48,000 each. As you will note, the noncompeting type 5 awards represent a substantial commitment of funds. As for the competing continuation grants, the so-called type 2's, there are, in fact, new grants in the sense of competition and could appropriately be considered in the same general category as the 11 new grants you referred to in your question.

Mr. Conte. How many grant applications were submitted to the Institute for 1974 funds?

Dr. Kreshover. A total of some 206 have been received to date. Of these, 99 new grants, or so-called type 1's, have been approved. The total number to be paid out of fiscal year 1974 funds, however, is not yet determined.

ORAL-FACIAL DEFECTS

Mr. Conte. What is the incidence of oral-facial defects in newborn infants?

Dr. Kreshover. The general figure we estimate for cleft lip and cleft palate is one in every 650 live births. However, our estimate for another important category of craniofacial defects, beyond the oral-facial clefting problem, is less reliable. Nevertheless, these complex and serious anomalies constitute a very real national problem with an incidence in this country of perhaps 20,000 victims. I referred to these last year, Mr. Conte, when your chairman commented on his receiving a communication from Dr. John Converse, Director of the New York University Institute for Plastic and Reconstructive Surgery. Doctor Converse and a few other leading surgeons in the world, are devoting much of their attention to the salvaging of babies and children who just a short time ago were being written off by society. This work is of vital importance, not alone because of the great contribution it makes to the alleviation of human suffering, but also because of the essential research information being provided to better understand the complex patterns and mechanisms of head and face growth and development, including the functions of speech, hearing, vision, and mastication.

Mr. Conte. How early can corrective surgery be undertaken now?

Dr. Kreshover. This will, of course, vary considerably with the individual case, and inasmuch as the defects we are thinking about are so very complex and individual, no general rule of thumb can be suggested, especially in the noncleft types of anomalies. Nevertheless, when considering the cleft lip alone, where bony growth and development is not directly involved, a surgical repair can often be completed when the infant attains a weight of about 10 pounds. The repair of any accompanying cleft palate must, on the other hand, be a matter of watchful diagnosis and far-reaching treatment planning by a team of experts, including orthodontists, speech physiologists and therapists, oral surgeons, pediatricians, psychologists, and others.

ACCELERATED DENTAL TRAINING

Mr. MICHEL. What progress has been made in the acceleration of dental training programs? Last year you spoke of programs beginning then that would complete the educational program in 3 years instead of 4. Are you actively involved in encouraging the development of programs of this type?

Dr. KRESHOVER. I do indeed recall commenting a year ago on the approaches by some dental schools to a so-called 3-year curriculum. While I am unable to cite the current situation, in the 1972–73 period there were 12 schools that had a 3-calendar-year educational program. It should be pointed out, however, that the student's experience in each of these schools continued to encompass 4 "academic years" by including the summer months in curriculum planning. With increasing concern about student enrollments and the need to graduate dentists, there may well be a trend toward more 3-year accelerated programs in dental schools.

With regard to the role of the NIDR in these kinds of programs, I should call your attention, Mr. Michel, to the fact that the Division of Dentistry in the Health Resources Administration has responsibility for dental education activities.

Mr. FLOOD. Thank you very much, Dr. Kreshover.

JUSTIFICATION OF THE BUDGET ESTIMATES

NATIONAL INSTITUTES OF HEALTH

National Institute of Dental Research

Amounts Available for Obligation 1/

	1974 Revised	1975
Appropriation..........................	$45,565,500	$43,959,000
Amount withheld (PL 93-192).........	-1,606,500	
Subtotal adjusted appropriation....	43,959,000	43,959,000
Real transfer to:		
"Departmental management"............ (For Department-Wide Reduction in Public Affairs)	-10,000	---
Comparative transfer to:		
"Office of Assistant Secretary for Health"......................... (Transfer of Administrative Support Activities to the Office of the Assistant Secretary for Health)	-31,000	---
"Departmental management"............ (Transfer of accounting functions from OS Working Capital Fund)	-4,000	---
Comparative transfers from:		
"Departmental management"............ (Transfer of indirect cost negotiation function to the OS Working Capital Fund)	+5,000	---
"National Institute of General Medical Sciences"................. (Decentralization of scientific evaluation grants program)	+36,000	---
Total, 1974 base obligations.......	43,955,000	43,959,000
Unobligated balance restored...........	6,134,000	---
Comparative transfer of restored obligated balance to Research Resources for General Research Support Grants.......................	-780,000	---
Total, obligations..................	49,309,000	43,959,000

1/ Excludes the following amounts for reimbursable activities carried out by this account: 1974 - $6,000; 1975 - $5,000.

Summary of Changes

1974 estimated obligations	$49,309,000
1975 estimated obligations	43,959,000
Net change	-5,350,000

	Pos.	1974 Amount	Change from 1974 Pos.	Change from 1974 Amount
Increases:				
A. Built-in:				
1. Extra day of pay		---		+17,000
2. Within grade increases		---		+95,000
3. FTS rate increase		---		+10,000
4. Postage increase		---		+8,000
5. Other (Rental, Utilities and increased costs of services and supplies)		---		+137,000
6. BEC Increase		---		+3,000
7. Annualization of 1974 pay increase		---		+167,000
8. Payment to "National Institutes of Health management fund" for centrally furnished services				+52,000
Subtotal		---		+489,000
B. Program:				
1. Research grants:				
a. Non-competing		9,599,000		+5,271,000
b. Competing		---		+1,646,000
c. Dental Research Institutes		6,850,000		+350,000
2. Fellowships		---		+821,000
Subtotal				+8,088,000
Total, increases		---		+8,577,000
Decreases:				
A. Built-in:				
1. Annualization of employment savings				-82,000
B. Program:				
1. Research grants:				
a. Non-competing		9,599,000		-3,870,000
b. Competing		5,059,000		-5,059,000
c. 1974 Obligations used to fund 1975 continuations		1,000,000		-1,000,000
2. Training grants:				
a. Regular		5,386,000		-2,001,000
b. 1974 Obligations used to fund 1975 continuations		240,000		-240,000
3. Fellowships (1974 Obligations used to fund 1975 continuations)		3,579,000		-1,500,000
4. Contracts		5,083,000		-175,000
Total, decreases				-13,927,000
Total, net change				-5,350,000

Explanation of Changes

Increases

A. Built-in: These increases will provide: 1. $17,000 for one extra day of pay in 1975; 2. $95,000 for within grade salary increases; 3. Increase of $10,000 for increase in cost of using Federal Telecommunications system; 4. Postage charges increase of $8,000; 5. $137,000 for Other increased charges, rentals. utilities and services and supply fund; 6. Increased charges of $3,000 for Bureau of Employee Compensation; 7. Annualization of 1974 pay increase of $167,000 and; 8. Payment of $52,000 to National Institutes of Health management fund for centrally furnished services.

B. Program

1. Research grants:
   a. The increase of $5,271,000 in non-competing research grants represent the continuation of previously awarded grants plus "new" continuations resulting from grants made in 1974. The number of continuations increased by 8 from 170 in 1974 to 178 in 1975.

   b. The amount of $1,646,000 in competing research grants reflects: (a) $500,000 for new awards (b) $1,146,000 for 24 competing continuations; an increase of $1,146,000 in competing continuations from 23 in 1974 to 24 in 1975.

   c. The increase of $350,000 for the Dental Research Institutes is for non-competing requirements.

2. Fellowships-increase of $821,000, of which $221,000 will support non-competing requirements and $600,000 is for new awards under the research fellowship training program.

Decreases

A. Built-in: - The decrease of $82,000 is for annualization of employment savings.

B. Program

1. Research grants:
   a. The decrease of $3,870,000 represents non-competing regular research grants that are being converted to competing status in 1975.

   b. The decrease of $5,059,000 reflects the completion or conversion of 73 competing grants to a non-competing status.

   c. The decrease of $1,000,000 reflects the reduced funding required in 1975 due to the multi-year funding of awards in 1974.

2. Training grants:
   a. The decrease of $2,001,000 consists of funds released from prior year.

   b. The decrease of $240,000 reflects the reduced funding required in 1975 due to the multi-year funding of awards in 1974.

3. Fellowships: The decrease of $1,500,000 reflects the reduced funding required in 1975 due to the multi-year funding of awards in 1974.

4. Research & development contracts: The decrease of $175,000 consists of funds released from prior year.

Obligations by Activity

Page Ref.		1974 Base * Pos.	1974 Base * Amount	1975 Estimate Pos.	1975 Estimate Amount	Increase or Decrease Pos.	Increase or Decrease Amount
138	Caries..................	34	$ 9,102,000 (10,112,000)	34	$8,995,000	---	-$107,000 A/
140	Periodontal and Soft Tissue Diseases.........		7,648,000 (9,462,000)		7,281,000		-367,000 B/
142	Restorative Materials.....		2,892,000 (3,252,000)		2,767,000		-125,000 C/
144	Craniofacial Anomalies....		6,180,000 (8,221,000)		6,099,000		-81,000 D/
146	Pain Control and Behavioral Studies......		998,000 (1,127,000)		966,000		-32,000 E/
148	Dental Research Institutes...............		6,850,000		7,200,000		+350,000 F/
150	Intramural Laboratory and Clinical Research........	165	7,282,000	165	7,596,000	---	+314,000 G/
152	Research Management and Program Services.........	69	3,003,000	69	3,055,000	---	+52,000 H/
	Total obligations (bases)	268	43,955,000	268	43,959,000	---	+4,000
	Total obligations........		(49,309,000)				

Explanation of Changes (by activity)

A/ Caries--decrease of $107,000. With the total funds provided research will continue within the broad framework of the four major program objectives. The most promising progress to date has been in the areas of (1) combating the microbiologic agent by chemotherapy and (2) increasing tooth resistance, primarily with new topical fluorides and adhesive tooth sealants.

B/ Periodontal and soft tissue diseases--decrease of $367,000. With the total funds available the projects to be developed will include specific studies aimed at plaque control. Research will focus on the development of better diagnostic methods for herpes simplex virus infections and on the search for suitable treatment methods for this disease. In addition research efforts will continue on the virology and immunology of this disease toward the development of a vaccine. Efforts will be made to conduct neoplastic diseases research with the medical community and the National Cancer Institute, particularly the regional cancer centers.

* 1974 Base - Excludes 1973 appropriation restorations. Total obligations shown in parentheses.

C/ Restorative materials--decrease of $125,000. With the total funds provided efforts will be continued to improve amalgams, composite resins, and other filling and adhesive materials; to evaluate different materials and designs for implants, and to develop materials to be used as artificial skin in maxillofacial prostheses.

D/ Craniofacial anomalies--decrease of $81,000. With the total funds available the concept of Craniofacial Anomalies centers to achieve a cohesive effort in investigations of all congenital craniofacial anomalies will be under exploration. This is timely because of the recent breakthrough in surgical procedures of severe craniofacial deformities and the achievements of the interdisciplinary research within the cleft palate centers.

E/ Pain control and behavioral studies--decrease of $32,000. With the total funds provided efforts will continue to develop as many aspects of complex and multifaceted pain problem as possible. High priority will continue to be given to the development of multidisciplinary and interdisciplinary pain centers in which major oral-facial pain problems can be studied at both basic and clinical levels.

F/ Dental research institutes--Increase of $350,000. The Dental Research Institutes will continue to build on and extend existing institutional research strengths; provide for participation of multiple disciplines, and facilitate collaboration of a wide range of biological, physical and social sciences in the study of oral health problems in relationships to the program objective of the NIDR.

G/ Intramural laboratory and clinical research--Increase of $314,000 will support built-in increases. With total funds provided the NIDR plans to expand research efforts in the general area of immunological mechanisms through basic and applied research, both in the laboratory and clinical facilities of the Institute, to determine the susceptibility of the individual to infection and disease. A continuing focus on plaque is essential to understanding both dental caries and periodontal disease. A Neurophysiology and Anesthesiology Program has been established to provide a primary setting for execution of much needed and basic and clinical research in problems of oral and facial pain. The primary interest in disordered facial and oral development remains that of determining mechanisms responsible for clefting of the lip and/or palate in man. It is from these inquiries that potential preventive and/or therapeutic technics may make themselves evident.

H/ Research management and program services--increase of $ 52,000 support built-in increases. Overall administration direction and coordination of the Institute programs will continue to be provided in 1975 with the funds available.

Obligations by Object

	1974 Estimate	1975 Estimate	Increase or Decrease
Total number of permanent positions............	268	268	--
Full-time equivalent of all other positions....	38	38	--
Average number of all employees................	311	311	--
Personnel compensation:			
Permanent positions........................	$5,078,000	$5,270,000	+$192,000
Positions other than permanent..............	324,000	329,000	+5,000
Other personnel compensation................	54,000	55,000	+1,000
Total personnel compensation..............	5,456,000	5,654,000	+198,000
Personnel benefits..........................	809,000	841,000	+32,000
Travel and transportation of persons..........	255,000	258,000	+3,000
Transportation of things......................	56,000	56,000	---
Rent, communications & utilities..............	192,000	210,000	+18,000
Printing and reproduction.....................	81,000	81,000	---
Other services:			
Project contracts..........................	5,083,000	4,908,000	-175,000
NIH management fund........................	2,346,000	2,398,000	+52,000
Other......................................	844,000	942,000	+98,000
Supplies and materials........................	870,000	876,000	+6,000
Equipment.....................................	465,000	465,000	---
Grants, subsidies & contributions.............	32,855,000	27,273,000	-5,582,000
Deduct quarters and subsistence charges.......	-3,000	-3,000	---
Total obligations by object.............	49,309,000	43,959,000	-5,350,000

Total obligations excluding
1973 appropriation......................($43,955,000)

Significant Items in House and Senate Appropriation Committee Report

Item	Action Taken or to be Taken
1974 Senate Report	
1. The Committee recommends that the uses of acupuncture for surgical analgesia and chronic pain be given additional consideration with regard to its effects on patients. Also recommended was an effort to inform professional and lay people of its feasibility and practicality. (Page 36)	1. Efforts have been directed at improving the pharmacologic aspects of oral facial pain control and exploring newer non-pharmacologic modalities such as acupuncture and electrical anesthesia.
2. The Committee recognizes that NIH has many inter-related health concerns and recommends that every attempt be made to utilize resources in inter-institute studies of common diseases. (Page 37)	2. The NIDR is currently coordinating and developing a program with the NCI to study oral cancer and periodontal diseases; with NIAID and NIAMDD on clinical and morphologic studies as well as biological projects in structure.
3. Two out of three middle-aged Americans suffer from periodontal disease. The Committee has provided additional resources to allow the Institute to press forward in this area. (Page 45)	3. The additional funds provided for the support of research on periodontal disease will expand the research efforts in area of immunological mechanisms.
4. Attention is now also being directed to other severe malformations of the face and head. The Committee is watching such developments with interest and has included additional funds to mount a significant program in this area. (Pages 45 and 46)	4. NIDR is initiating additional research focused on the understanding of the basic mechanisms of craniofacial anomalies in man with the aim toward prevention.

Authorizing Legislation

Legislation	1975 Authorization	 Appropriation Requested
Public Health Service Act		
Section 301--Research and Investigation, in general..	Indefinite	
		$43,959,000
Title IV, Part C--National Institute of Dental Research..	Indefinite	

National Institute of Dental Research

Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
1965	$19,455,000	$19,336,000	$19,339,000	$19,339,000
1966	21,306,000	21,306,000	22,624,000	22,723,000
1967	23,783,000	27,229,000	27,229,000	27,229,000
1968	29,013,000	29,013,000	30,775,000	29,009,000
1969	29,220,000	28,359,000	29,222,000	28,789,500
1970	28,095,000	28,095,000	30,685,000	29,689,831
1971	33,606,000	34,085,000	35,085,000	34,229,000
1972	37,921,000	40,788,000	43,788,000	42,348,000
1973*	39,311,000	45,836,000	52,845,000	45,836,000
1974**	38,448,000	44,127,000	46,996,000	45,561,500
1975	43,959,000			

*Note: This appropriation authority was the continuing resolution. The appropriation amount was the House Allowance, which was the lower of the House or Senate amounts in the first vetoed bill.

** Appropriation after reduction, $43,955,000.

National Institute of Dental Research

	1974 Base *		1975 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits...........	268	$6,262,000	268	$6,492,000	---	+$230,000
Other expenses...........	---	37,693,000	---	37,467,000	--	-226,000
Total..................	268	43,955,000	268	43,959,000	--	+4,000

General Statement

As the chief sponsor of dental research and related training in the United States, the Institute encompasses a broad field of activities and studies, ranging from causes of dental and other oral diseases to the development and application of more effective therapeutic and preventive measures.

Because of their complexity, oral problems must be attacked through a comprehensive program of laboratory, clinical, field, and epidemiological studies in such varied areas as developmental biology, genetics, microbiology, virology, and materials science. In fact, the efforts of over 30 scientific disciplines are today contributing to an ever-growing base of information on which NIDR is building improved means to treat and prevent disease.

To expand the dental research base NIDR developed five Dental Research Institutes and Centers which bring together all of the appropriate resources of the parent universities and focus these resources upon the problems of oral health in an ideal research and training environment. The Institutes and Centers have created a sufficiently stimulating atmosphere to attract investigators and students from disciplines not generally associated with dental research. Until these Institutes were created, the NIDR was the only broad based dental research institute in the United States.

Prevention is of crucial importance in dentistry because, unlike medicine's brilliant successes with cures, oral health problems are largely irreversible. The major programs of NIDR are concerned with dental caries (tooth decay); periodontal (gum) disease; problems of growth and development, especially cleft lip and palate and malocclusion; and a variety of oral lesions affecting the tongue, cheeks, and lips. Other areas of emphasis are the development of improved restorative materials, including successful tooth implants, and pain control.

Tooth decay, one of the Institute's main concerns, afflicts nearly everybody. Late in FY 1971 the National Caries Program became operational. This intensified research and development effort in intramural, collaborative (contract), and grant-supported research is designed to develop methods to eliminate caries as a major health problem.

Gum diseases, collectively referred to as periodontal disease, are as widespread and serious as tooth decay: about 20 million people have lost all their teeth as a result of them; two out of three middle-aged Americans suffer from them. Research to overcome periodontal disease is a second major target area of the Dental Institute. A number of significant research leads should provide sufficient new data upon which to base increased future efforts directed specifically toward developing improved preventive or therapeutic measures.

* Excludes 1973 appropriation restorations.

DHEW- National Insitutes of Health
CROSSWALK - 1974 COLUMN 1975 PRESIDENT'S BUDGET

INSTITUTE: National Institute of Dental Research
(In Thousands)

Program	Research Grants						Laboratory and Clinical Research	Research and Development Contracts	Other Direct Operations	Total
	Regular Program		Specials		Training Programs					
	Non-competing	Competing	Multi-disciplinary Centers	Other	Grants	Fellowships				
1974 Base Obligations										
1. Caries............	2,896	1,376		145	135	464		3,000	1,086	9,102
2. Periodontal and Soft Tissue Diseases....	3,017	1,191		295	1,370	1,360		415		7,648
3. Craniofacial Anomalies..........	2,879	393	342	162	1,368	806		230		6,180
4. Restorative Materials..........	686	536		87	339	81		1,163		2,892
5. Pain Control and Behavioral Studies.	121	304		111	173	189		100		998
6. Dental Research Institutes.........			6,850							6,850
7. Intramural Laboratory and Clinical Res.,.							7,282			7,282
8. Research Management and Program Srv....									3,003	3,003
Subtotal...........	9,599	3,800	7,192	800	3,385	2,900	7,282	4,908	4,089	43,955
Unobligated Balance Restored										
1. Caries..............		674			110	51		175		1,010
2. Periodontal and Soft Tissue Diseases....		541			937	336				1,814
3. Craniofacial Anomalies..........		938			841	262				2,041
4. Restorative Materials..........		70			280	10				360
5. Pain Control and Behavioral Studies.		36			73	20				129
Subtotal...........		2,259			2,241	679		175		5,354
Total Obligations......	9,599	6,059	7,192	800	5,626	3,579	7,282	5,083	4,089	49,309

DHEW- National Insitutes of Health

CROSSWALK - 1975 COLUMN 1975 PRESIDENT'S BUDGET

INSTITUTE: National Institute of Dental Research
(n Thousands)

	Research Grants									
			Specials							
	Regular Program		Multi-disciplinary		Training Programs		Laboratory and Clinical	Research and Development	Other Direct	
Program	Non-competing	Competing	Centers	Other	Grants	Fellowships	Research	Contracts	Operations	Total
1. Caries...............	3,600	524		145	135	464		3,000	1,127	8,995
2. Periodontal and Soft Tissue Diseases....	3,310	531		295	1,370	1,360		415		7,281
3. Craniofacial Anomalies..........	2,900	291	342	162	1,368	806		230		6,099
4. Restorative Materials...........	925	172		87	339	81		1,163		2,767
5. Pain Control and Behavioral Studies.	265	128		111	173	189		100		966
6. Dental Research Institutes..........			7,200							7,200
7. Intramural Laboratory and Clinical Res...							7,596			7,596
8. Research Management and Program Srv....									3,055	3,055
Total obligations......	11,000	1,646	7,542	800	3,385	2,900	7,596	4,908	4,182	43,959

Appropriation
Budget Mechanism

	1974 Base *		1975	
	Number	Amount	Number	Amount
Grants				
Regular				
Non-competing	170	$9,599	178	$11,000
Competing	20	2,444	24	1,146
New	36	1,136	11	500
Supplemental	(6)	220	0	0
Subtotal	226	13,399	213	12,646
Special				
Special				
Specialized Research Centers	1	342	1	342
Dental Research Institutes	5	6,850	5	7,200
Research Career Program	73	764	73	764
Scientific Evaluation	1	36	1	36
Subtotal	80	7,992	80	8,342
Total Grants	306	21,391	293	20,988
Fellowships				
Non-competing	18	220	140	2,300
Competing	4	120	0	0
New	140	2,460	40	600
Supplemental	(2)	100	0	0
Subtotal	162	2,900	180	2,900
Training Grants				
Non-competing	36	2,477	43	2,785
Competing	7	308	0	0
New	0	0	0	0
Supplemental	(24)	600	(24)	600
Subtotal	43	3,385	43	3,385
Laboratory and Clinical Research		7,282		7,596
Research & Development Contracts		4,908		4,908
Collaborative Research and Support		1,086		1,127
Research Management & Program Services		3,003		3,055
TOTAL		43,955		43,959

*Excludes 1973 appropriation restorations.

Caries

Authorizing Legislation: Public Health Service Act, Title IV, Part C

	1974 Base *		1975 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits............	34	$900,000	34	$930,000	---	+$30,000
Other expenses............		8,202,000		8,065,000		-137,000
Total............	34	9,102,000	34	8,995,000	---	-107,000

Budget Mechanism:	1974 Base *	1975 Estimate	Increase or Decrease
Research Grants:			
Regular...............	4,272,000	4,124,000	-148,000
Special...............	145,000	145,000	0
Subtotal............	4,417,000	4,269,000	-148,000
Fellowships.............	464,000	464,000	0
Training grants.........	135,000	135,000	0
Research and Development Contracts..............	3,000,000	3,000,000	0
Collaborative Research and Support............	1,086,000	1,127,000	+41,000
Total............	9,102,000	8,995,000	-107,000

Objectives, 1975:

In 1971, additional funds were authorized to develop the National Caries Program (NCP), a highly organized research and development effort intended to develop methods to eliminate caries as a major health problem. Research grants, research contracts, direct operations research, graduate training grants, fellowships, and research career program awards are used to accomplish program goals.

Research will continue within the broad framework of the four major program objectives. The most promising progress to date has been the areas of (1) combating the microbiologic agent by chemotherapy and (2) increasing tooth resistance, primarily with new topical fluorides and adhesive tooth sealants. A large clinical testing program will be initiated to evaluate the ability of several antimicrobial agents to control human dental plaque under standardized, controlled conditions. Laboratory and animal screening of new compounds will continue. Several new topical fluorides appear to have antimicrobial properties as well. At least two of these will undergo large-scale clinical trials in 1975. Increased emphasis will be placed upon gathering detailed cost/benefit data when anti-caries agents are used in school-based preventive programs.

Following preliminary, but promising success in partial immunization of laboratory animals against caries, the Program will intensify research to establish the feasibility of this route to caries prevention. Contracts will be awarded to establish a primate testing facility and to systematically identify antigenic components of oral microorganisms.

* Excludes 1973 appropriation restorations.

Accomplishments 1974

Dental caries is localized, progressive destruction of the teeth initiated by acid demineralization of the outer tooth enamel. It results from a complex interaction among three factors: bacterial agents, dietary environment, and tooth susceptibility. The general operating plan of the National Caries Program embraces four major objectives or strategies.

I. To Combat the Microbial Agent. In FY 1974, the Program supported 16 research projects on microbial aspects of dental caries, including epidemiology, development of control measures, and clinical testing of control measures. Currently, research is concentrated on exposed surface root caries; however, research on caries of root surfaces is expanding. Dentists and oral health scientists have been aware that as teeth last longer caries of the root surface, usually associated with periodontal disease, is more frequently observed. One study is designed to determine the prevalence of this form of caries.

II. To Increase the Resistance of the Tooth. It is commonly held that the caries-inhibitory effect of direct applications of fluoride to teeth increases with the amount of fluoride that becomes associated with the enamel surface and the depth of fluoride penetration. These relationships need to be examined in detail and related to mechanisms of fluoride anti-caries action and to technics that increase fluoride uptake by enamel.

During FY 1973, support was provided through contracts for four clinical trials on efficacy and mechanism of different topical fluoride treatments, and two projects to analyze the fluoride content of enamel samples. Polymer films also appear promising in protecting the tooth surface, particularly in the pit and fissure areas. The Program therefore, has contracted for three longitudinal studies under conditions resembling possible eventual public health use of these agents. The questions under evaluation include the amount of training that is necessary to apply the sealant. Data from these studies, now entering their third year, show that differences in technic of application cause large differences in sealant retention and that some sites are considerably more difficult to seal than others. In general, however, this approach to caries control shows considerable promise.

III. To Modify the Diet. Caries control through decreased consumption of sucrose is made difficult because of public predilection for sweet foods, patterns of snack food consumption, and agricultural, food processing, and marketing patterns based on sucrose. Through twelve contracts, new sweeteners (both carbohydrate and noncarbohydrate) are being investigated, and new formulae and processes are being developed to lower the sucrose content of high-sucrose foods. An evaluation is being made of food characteristics that magnify the cariogenicity of snacks, and dietary additives are being developed to make sucrose less cariogenic in foods.

IV. To Develop Methods to Improve Delivery and Acceptance of Caries Prevention Technics. As caries prevention measures are developed, provision must be made to insure their acceptance and utilization. Many factors affect the utilization of newly developed agents and treatment plans such as perceived health status and benefits, costs to individuals in public health programs, and ease and attractiveness of use. Currently, three contract studies are in progress to evaluate the benefit, cost and acceptance of specific preventive treatment regimens in school children. Educational programs to encourage greater concern for tooth care are included in the protocols.

In addition, a behavioral motivation program of oral hygiene instruction and family encouragement is being tested, and a contract has been awarded to develop a prognostic test for caries. Based upon correlations between plaque microbiology and metabolic characteristics and developing caries, scientists will attempt to design a test to predict caries in children. This test should have value in predicting certain types of caries in adults.

Periodontal and Soft Tissue Diseases

Authorizing Legislation: Public Health Service Act, Title IV, Part C

	1974 Base *		1975 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits...........	---	---	---	---	---	---
Other expenses...........		$7,648,000		$7,281,000		-$367,000
Total............	---	7,648,000	---	7,281,000	---	-367,000
Budget Mechanism:						
Research Grants:						
Regular...............		4,208,000		3,841,000		-367,000
Special...............		295,000		295,000		0
Subtotal...........		4,503,000		4,136,000		-367,000
Fellowships............		1,360,000		1,360,000		0
Training grants.........		1,370,000		1,370,000		0
Research and Development Contracts..............		415,000		415,000		0
Total...........		7,648,000		7,281,000		-367,000

Objectives, 1975:

The ultimate mission of the Periodontal and Soft Tissue Diseases Program is to develop new knowledge which may lead to the prevention and eradication of these diseases. Research grants, research contracts, graduate training grants, fellowships, and research career program awards are used to accomplish program goals.

Continued emphasis will be placed on defining the numerous steps in the periodontal disease process itself, as well as other soft tissue lesions, in order to develop more rational means for their prevention and control. The periodontal projects to be developed will include specific studies aimed at plaque control. Thus, a variety of antibacterial compounds will be tested for efficacy against dental plaque formation.

Ongoing studies designed to develop fundamental knowledge necessary to control the tissue destructive aspects of the immune and the inflammatory response also will receive strong support. Toward this end, studies of patients with specific immune deficiencies will be initiated. It is hoped that such efforts will clarify the role of immune mechanisms in periodontal diseases.

Increased programming efforts will also be made to stimulate research dealing with aphthous ulcers, herpes virus infections, and oral cancer. In particular, research will focus on the development of better diagnostic methods for herpes simplex virus infections and on the search for suitable treatment methods for this disease. In addition, research efforts will continue on the virology and immunology of this disease, with the objective of developing a vaccine for ultimate prevention. Parallel emphasis will be given to the problem of oral cancer. In order to develop a more coordinated effort in the study of

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* Excludes 1973 appropriation restorations.

this important area of neoplastic diseases efforts will be made to work with the medical community, with the National Cancer Institute, and particularly with the regional cancer centers.

Accomplishments 1974

Periodontal Disease

Periodontal (gum) disease ranks as a major oral health problem. Actually, it is a group of diseases, rather than a single entity. The onset, which may occur as early as childhood or adolescence, is known as gingivitis, or inflamed gums. With good oral hygiene, most of the early cases can be reversed. However, as the disease progresses, reversal is less likely. If the disease is allowed to progress unchecked, it results in destruction of the bone supporting the teeth with the eventual loss of the teeth.

Treatment of periodontal disease is time consuming, costly, frequently unsuccessful, and remains essentially unavailable to the majority of the population because of the high cost and the shortage of periodontists. Thus, to eliminate the harmful effects of this disease and thereby improve the quality of life, preventive measures easy enough for everyone to employ must be developed. In order to provide us with an understanding of the disease processes, the major research efforts in periodontal diseases have involved studies on pathogenesis response and the mechanisms of tissue destruction. Nevertheless, a significiant amount of attention has also been devoted to etiologic factors, with the main emphasis being in the area of microbiology and dental plaque formation.

Since the dentobacterial plaque is thought to initiate the chain of events leading to inflammation and bone destruction, etiologic studies have emphasized its role in disease. In the last few years, efforts to identify pathogenic bacteria have become systematic and comprehensive. It is now becoming clear that different forms of periodontal disease may be caused by different bacteria. New information on mechanisms of tissue destruction that may operate in periodontal disease has provided evidence that the net loss of connective tissues observed is probably the result of depressed formation as well as enhanced degradation. Emerging evidence indicates that the inflammatory process offers mechanisms which bring about both of these effects. Efforts to develop suitable animal models for periodontal disease studies have been encouraging. Although research efforts dealing with the prevention and treatment of periodontal disease have been at a low level in the past, studies of the etiology and pathogenesis of the disease have yielded sufficient new data upon which to base increased future efforts directed specifically toward developing improved preventive or theraputic measures.

Oral Cancer

Since there has been little oral cancer research at NIH in the past, NIDR and the National Cancer Institute now have an agreement to cooperate in stimulating research in this important area. This beneficial arrangement provides the means whereby NIDR and NCI can work together in many ways to foster oral cancer research.

Herpes Simplex Virus

The control of herpes simplex virus infections and other oral ulcerative diseases is an important research target. NIDR believes that better diagnosis, control, and prevention of herpes simplex virus infections can be realized within a forseeable period through more intensified research. The recent significant advances in viral immunology may well provide new approaches to the treatment of herpes simplex virus infection and may offer clues for the development of an effective vaccine. In addition, it is believed that increased research with modern sophisticated methods may reveal the causes of other common painful oral ulcerative diseases, such as recurrent aphthous ulcers. With this knowledge, additional research can be initiated to develop the means to control these diseases.

Restorative Materials

Authorizing Legislation: Public Health Service Act, Title IV, Part C

	1974 Base *		1975 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits...........	---	---	---	---	---	---
Other expenses...........		$2,892,000		$2,767,000		-$125,000
Total...........	---	2,892,000	---	2,767,000	---	-125,000

Budget Mechanism:	1974	1975	Increase or Decrease
Research Grants:			
Regular..............	1,222,000	1,097,000	-125,000
Special..............	87,000	87,000	0
Subtotal...........	1,309,000	1,184,000	-125,000
Fellowships............	81,000	81,000	0
Training grants.........	339,000	339,000	0
Research and Development Contracts.............	1,163,000	1,163,000	0
Total...........	2,892,000	2,767,000	-125,000

Objectives, 1975:

Since the highly specialized tissues of the mouth cannot replace themselves when they are lost, treating the effects of dental disease is still largely based upon the effective use of available materials. Therefore, the principal objectives of the Restorative Materials Program are to provide better dental care by fostering the development of improved materials and methods to restore lost oral tissues to normal form and function. Research grants, research contracts, graduate training grants, fellowships, and research career program awards are used to accomplish program goals.

Efforts will be continued to improve amalgams, composite resins, and other filling and adhesive materials. In the immediate future the Restorative Materials Program will give special emphasis to research on artificial dental implants and will attempt to initiate projects to develop better maxillofacial prostheses. Through contract mechanisms the program is presently following a more systematic approach to the research and development of implants than has been attempted previously. It is expected that three significant contracts will provide solid progress towards achieving an effective implant. In one contract the influence of tooth design on implant acceptability will be studied in animals. In this study the effects of tooth shape, as well as the effects of grooves, slots, and porosity will be evaluated. In the other two studies, the influence of the chemical composition of the tooth implant will be assayed. Artificial teeth made of ceramic, metal, and plastic will be tested under these contracts.

Accomplishments 1974:

The Restorative Materials Program supports research in five broad categories: restorative materials for repairing the damage from dental

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* Excludes 1973 appropriation restorations.

diseases; plastic adhesive sealants for protecting the surfaces of teeth against decay and for sealing the margins of fillings; maxillofacial prostheses for replacing tissue defects and mutilations resulting from birth defects, accidents, or surgery; artificial tooth implants to provide either serviceable replacements for missing teeth, or posts to anchor bridges or complete dentures in place; and development of devices, equipment, and standards for materials.

About 25 percent of the total funds in FY 1974 was expended for research to improve or develop new filling materials, about 25 percent to continue projects dealing with adhesives, about 20 percent on implant investigations, and 20 percent for studies on maxillofacial prostheses.

Targeted efforts by contracts involving the study of marine animal adhesives have been concluded with the partial analysis of the proteinaceous cement secretions of barnacles and mussels, and preliminary characterization of the material. Retentive tests indicate that these materials are no better than synthetic products currently available. Future studies on marine animal adhesives will be supported only through research grants. In the meantime promising synthetic elastomeric liners for cavity preparations are being evaluated *in vivo* in teeth of dogs and monkeys utilizing composite and also amalgam restorations.

Craniofacial Anomalies

Authorizing Legislation: Public Health Service Act, Title IV, Part C

	1974 Base *		1975 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits	---	---	---	---	---	---
Other expenses		$6,180,000		$6,099,000		-$81,000
Total	---	6,180,000		6,099,000		-81,000
Budget Mechanism:						
Research Grants:						
Regular		3,272,000		3,191,000		-81,000
Special		504,000		504,000		0
Subtotal		3,776,000		3,695,000		-81,000
Fellowships		806,000		806,000		0
Training grants		1,368,000		1,368,000		0
Research and Development Contracts		230,000		230,000		0
Total		6,180,000		6,099,000		-81,000

Objectives, 1975:

Research grants, research contracts, graduate training grants, fellowships, and research career program awards are used to accomplish program goals.

The concept of Craniofacial Anomalies Centers to achieve a cohesive effort in investigations of all congenital craniofacial anomalies will be under exploration. This is timely because of the recent breakthrough in surgical procedures of severe craniofacial deformities and the achievements of interdisciplinary research within the cleft palate centers. In addition to the more radical surgery, surgical-orthodontic experiments on subhuman primates will quantitatively investigate the reinnervation and revascularization of tissue following maxillotomy procedures. The control and guidance of craniofacial growth through orthopedic measures will be explored in research and assessed in a state-of-the-art workshop. Teratogenic studies on cleft lip and palate will focus on the activity of enzymes, drugs and environmental factors on palatal closure. These studies will be done on experimental animals, and it is planned that studies of high risk mothers and discordant monozygotic twins will be started to provide definitive information about the multifactorial etiological factors in humans.

Accomplishments 1974:

Currently craniofacial anomalies research of the Institute is focused on improvement and extension of treatment and understanding of the basic mechanisms as an aim toward prevention of such developmental aberrations in man.

* Excludes 1973 appropriation restorations.

The Program comprises three major areas (a) congenital malformations such as cleft lip/palate and other syndromes which may involve numerous craniofacial structures: (b) acquired malformations from surgery or accidents, and (c) malocclusion of teeth and jaws. In addition, fundamental research in prenatal and postnatal developmental biology is supported.

A more precise understanding of the roles of environment and genetics in developing the final form and function of oral-facial structures has been reached. It is now believed that the potential for modifying the growth and alignment of teeth and jaws is greater than was thought to be true earlier. Thus, the stage is set to attempt to intercept or prevent certain malocclusions by applying local forces to guide growth in a favorable manner.

Genetic-epidemiological studies are in progress to identify factors contributing to the incidence of oral-facial abnormalities. These studies will investigate possible teratogens or nutritional factors in abnormalities as well as genetic and maternal influences.

Experimental approaches to the study of oral-facial abnormalities are greatly advanced. New methods are available to study the development of oral-facial tissues of experimental animals in organ culture. Specific teratogens have been identified which produce defined abnormalities in animals. Important events in tissue development have been identified. Such studies will permit the classification of human disorders in biochemical terms.

Studies on experimental surgical procedures and wound healing have provided sound data upon which to base treatment technics which will lead to better control of bone growth in the habilitation of congenital anomalies. Studies in subhuman primates are providing valuable information on revascularization and reinnervation of component skeletal fragments which have been surgically repositioned.

Pain Control and Behavioral Studies

Authorizing Legislation: Public Health Service Act, Title IV, Part C

	1974 Base *		1975 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits............	---	---	---	---	---	---
Other expenses............		$998,000		$966,000		-$32,000
Total............	---	998,000		966,000		-32,000
Budget Mechanism:						
Research Grants:						
Regular................		425,000		393,000		-32,000
Special...............		111,000		111,000		0
Subtotal............		536,000		504,000		-32,000
Fellowships.............		189,000		189,000		0
Training grants.........		173,000		173,000		0
Research and Development Contracts..............		100,000		100,000		0
Total............		998,000		966,000		-32,000

Objectives, 1975:

The program title indicates its dual nature. The pain control activity represents the major portion of the program and deals with continuing efforts to increase knowledge concerning the nature, etiology, pathophysiology, diagnosis and treatment of the major pain problems associated with the oral-facial region, including the fear and anxiety complex generated by the anticipation of pain in the routine dental treatment situation. The behavioral studies component of the program encompasses efforts to achieve greater utilization of behavioral sciences knowledge in the understanding and alleviation of a variety of dental and oral problems. Mechanisms available to accomplish these program goals include support via research grants and contracts, the training of research manpower and the convening of special workshops, conferences and symposia to assess the current state of knowledge and to chart future research directions.

Efforts will continue to develop as many aspects of the complex and multifaceted pain problem as possible. High priority will continue to be given to the development of multidisciplinary and interdisciplinary pain centers in which major oral-facial pain problems can be studied at both basic and clinical levels. The NIDR Dental Research Institutes will be utilized as additional resources for pain and behavioral research.

As acupuncture research projects are initiated, it is anticipated that new light will be shed on the mystery of this significant and intriguing phenomenon. Continued efforts will be made to develop further the potential of electrical anesthesia.

* Excludes 1973 appropriation restorations.

In the behavioral studies area, efforts will be made to initiate studies for the more reliable evaluation of an individual's dental fears and anxiety so that more effective methods for their control and reduction can be developed.

The Pain Control and Behavioral Studies Program will continue to inventory and coordinate the behavioral content of all NIDR program areas and provide assistance in project development and evaluation. Advice and assistance will be provided to these other program areas and basic behavioral research projects will be identified to provide information relevant to a variety of dental disease problems.

Accomplishments 1974:

A. Pain Control - The avoidance and relief of pain continue to be major health concerns of the American people and, when related to the oral-facial area, of special interest to NIDR. Efforts continue to increase knowledge of those aspects of the overall pain problem relevant to the mission of NIDR. These include the fear and anxiety associated with anticipated dental treatment, the management and control of pain inherent in most dental procedures and the wide variety of oral-facial pain symtomatic syndromes such as tic douloreaux, temporomandibular joint syndrome, atypical facial pain, and others. Efforts have been directed at improving the pharmacologic aspects of pain control and exploring newer non-pharmacologic modalities such as acupuncture and electrical anesthesia.

Basic research on oral-facial mechanisms of pain has led to the development of a behavioral model in non-human primates which appears to resemble human responses to tissue-threatening or tissue-damaging stimuli. Such research provides a basic framework in which mechanisms of oral-facial pain as well as new methods of pain control can be studied intensively. During the past year, significant progress has been made in treating one type of facial pain known as the myofacial pain dysfunction syndrome (MPD) utilizing a combination of behavioral and pharmacologic approaches that in one major study has resulted in an 80% success rate. Other studies have focused on increasing the safety of nitrous oxide analgesia by an intensive investigation of its cardiovascular effects at various nitrous oxide-oxygen combinations. Progress has been reported in more basic investigations studying the ways in which stimuli from the trigeminal nerve and the tooth pulp are processed in the brain. Of major significance has been the successful NIDR staff programming of a study to be initiated in the near future to determine the mechanism of acupuncture analgesia and to evaluate its effectiveness in the treatment of severe dental pain.

B. Behavioral Studies - With increasing recognition of the importance of the behavioral aspects of many dental problems, efforts continue to utilize the behavioral sciences more effectively in these situations. A comprehensive review is underway of the fear and anxiety syndrome responsible for avoidance by millions of essential dental treatment and a workshop is planned for the near future to identify new approaches toward a solution of this avoidance phenomenon.

Dental Research Institutes

Authorizing Legislation: Public Health Service Act, Title IV, Part C

	1974 Base *		1975 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits...........	---	---	---	---	---	---
Other expenses...........		$6,850,000		$7,200,000		+$350,000
Total.............	---	6,850,000		7,200,000		+350,000
Budget Mechanism:						
Research Grants:						
Special...............		6,850,000		7,200,000		+350,000
Total...........		6,850,000		7,200,000		+350,000

Objectives, 1975:

The underlying idea was to plan and develop Institutes or Centers which would bring together all of the appropriate resources of the parent universities and focus these resources upon the problems of oral health in an ideal research and training environment. It is expected that the Institutes and Centers would create a sufficiently stimulating atmosphere to attract investigators and students from disciplines not generally associated with dental research. Until these Institutes were created, the NIDR was the only broad dental research institute in the United States. NIDR awards research grants annually to five universities to support the Institutes/Centers.

Plans for a comprehensive evaluation of the institute/center concept are well into the formulative stage. Details for the study should be completed within the next few months, and the actual evaluation should be completed in 1976.

This special activity is intended to achieve the most from existing dental research capability and also to develop new manpower resources by challenging scientists from medical, engineering, and graduate schools, as well as other university components. Institutes are expected to build on and extend existing institutional research strengths; provide for participation of multiple disciplines, and facilitate collaboration of a wide range of biological, physical, and social sciences in the study of oral health problems in relationships to the program objectives of the NIDR. Interaction with the educational programs of the parent university is encouraged by having an appreciable component of Institute research staff serve as active members of the academic departments representing their fields of competence. Although each Institute requires a permanent staff, participation by other scientist on a temporary or part-time basis is strongly encouraged. Institutes are also encouraged to establish mutually beneficial relationships with other regional resources including educational and research institutions, hospitals, computer facilities, MEDLARS regional centers, and primate centers.

* Excludes 1973 appropriation restorations.

Accomplishments 1974:

In 1974 NIDR will award five research grants, amounting to $6,850,000 to five universities for the support of Institutes/Centers. The current year has been a period of maturation and stabilization for the four Institutes/Centers at the Universities of Alabama, North Carolina, Pennsylvania, and Washington. However, the Institute at the University of Michigan has undergone a major reorganization under the leadership of a new Director. Its investigators have been grouped into three interdisciplinary teams to tackle three major problem areas of oral health: (1) periodontal disease and caries, (2) viral diseases of the oral cavity, and (3) growth and function of the masticatory apparatus. Although Centers at the University of North Carolina and the University of Pennsylvania will acquire new directors this year, it is not anticipated that they will make major revisions in their research programs.

Several young investigators, attracted to dental research by the institute environment, have become recognized as established investigators in their respective disciplines as well as in oral health research. In addition, students are being attracted in increasing numbers to laboratories of the institutes. Both of these facts are indicators of high quality research in the centers.

Many important collaborative research projects have been developed between center scientists and other researchers at local, regional, national, and international levels. However, it is hoped that more interaction between institutes and dental schools can be promoted. To stimulate interest on the part of dental schools, NIDR collected descriptive materials from each of the five centers and mailed copies to all of the dental schools, dental clinics, and graduate schools of dentistry in the United States. The Center for Oral Health Research at the University of Pennsylvania announced a Visiting Scientist Program, and the Dental Research Center at the University of North Carolina invited a representative from each of the southeastern dental schools to visit the Center and present a seminar to its investigators. Hopefully, some good collaborative programs will result from these efforts.

Intramural Laboratory and Clinical Research

Authorizing Legislation: Public Health Service Act, Title IV, Part C

	1974 Base *		1975 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits...........	165	$3,025,000	165	$3,169,000	--	+$144,000
Other expenses...........		4,257,000		4,427,000		+170,000
Total...........	165	7,282,000	165	7,596,000	--	+314,000

Objectives, 1975:

The laboratory and clinical research studies of the Institute are concerned with the causes, treatment, control, and prevention of diseases and disorders of the oral cavity and facial region, e.g. dental caries, periodontal disease, and oral-facial birth defects. Treatment, control and prevention of oral disorders and diseases are explored through basic and applied research in the laboratory and clinical facilities of NIDR. When required and properly justified, contracts are used to support certain aspects of direct operations research.

In FY 1975, the NIDR plans to expand research efforts in the general area of immunological mechanisms. In the aggregate, these mechanisms determine the susceptibility of the individual to infection and disease. Such "host factors" have now been clearly demonstrated to play specific and essential roles in the etiology and pathogenesis of oral diseases, especially periodontal disease, herpes simplex infections, and aphthous stomatitis. It now appears particularly appropriate to extend and apply our current base of immunological information, heretofore derived primarily from animal experimentation, to the various clinical disease states in man.

The Institute's long standing interest in the nature of dental plaque will continue to receive emphasis. The nature of plaque, particularly the complex interplay between the microorganisms harbored by plaque, seem to determine its pathogenicity both with respect to dental caries and to periodontal disease. Accordingly, a continuing focus on plaque is essential to understanding both disease states. In conjunction with the Institute's National Caries Program, intramural effort will be directed toward characterization of particular strains of bacteria in the plaque, with the intent of developing specific therapeutic agents or technics against them.

An increased capacity is planned for dealing with problems of oral and facial pain, i.e. a Neurobiology and Anesthesiology Program has been established to provide much needed basic and clinical research in these areas. Our approach to elucidation of problems relating to pain and pain control will continue to be a dual one, i.e. fundamental research in the neurological basis of facial pain, combined with systematic scrutiny of new analgesic and anesthetic agents at the clinical level.

Disordered facial and oral development remains one of the most tragic and difficult problems facing dental research. Laboratory and clinical programs will continue to explore from every point of view the nature of human development both at the cellular and molecular level as well as in experimental

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* Excludes 1973 appropriation restorations.

animal models and human patients. While our primary interest remains that of determining mechanisms responsible for clefting of the lip and/or palate in man (a birth defect occurring in approximately 1 out of 700 live births in the United States), our attention must necessarily also be directed to broader research questions relating to the nature of growth and differentiation, since it is from these inquiries that potential preventive and/or therapeutic technics may make themselves evident.

Accomplishments 1974:

In Fiscal Year 1974, approximately 114 research projects will be supported at a cost of $7,282,000.

Notable progress has been made in the systematic exploration of host factors in the development of periodontal disease. These immunological mechanisms dictate the host's response to the noxious agent (dental plaque), which is presumed to be responsible for the genesis of periodontal tissue destruction, and so appear to determine the gravity of the disease as well as its course of progression. While it is clear that no periodontal involvement occurs in a mouth free of dental plaque, information regarding the host's reaction to the plaque seems very likely to provide possible routes for preventive measures. Such approaches are essential in combatting the disease, since efforts to maintain the mouth in a plaque-free status through conventional educational technics of oral hygiene appear to be unrealistic.

In another area, laboratory and clinical research into the factors controlling infections by herpes simplex virus have been much expanded. Particularly notable has been the demonstration that the virus is capable of spreading directly from an infected cell to its neighbors without exposing itself to the extracellular environment. This mode of transmission explains in part why the herpes virus is difficult to combat with conventional therapeutic approaches or by the individual's own defense mechanisms, both of which usually depend upon extracellular exposure for their effectiveness.

Clinical research has also continued to be rewarding in the area of salivary gland function, particularly with regard to the utility of minor salivary gland biopsies in diagnosing and assessing therapeutic effectiveness in patients with Sjogrens syndrome.

Finally, research findings concerning the mechanism of synthesis and aggregation of the fibrous protein collagen (the predominant supporting matrix of bones and teeth), which have been the subject of continuing scrutiny at NIDR for a decade, are now being extended to levels of clinical application. A wide variety of genetically determined disease states in man and animals have now been demonstrated to reflect disordered pathways of collagen synthesis or, more frequently, inadequate aggregation of the collagen molecules into functional collagen fibers.

Research Management and Program Services

Authorizing Legislation: Public Health Service Act, Title IV, Part C

	1974 Base *		1975 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits............	69	1,531,000	69	$1,587,000	---	+$56,000
Other expenses............		1,472,000		1,468,000		-4,000
Total............	69	3,003,000	69	3,055,000	---	+52,000

Objectives 1975

In 1975, this activity will continue to provide for the overall administration, direction, and coordination of the Institute's programs.

This activity funds: (1) The Director and his immediate staff concerned with administrative management, financial management, program planning and evaluation, and computer processing services, and (2) the scientific and administrative staff responsible for grant and contract programming, review and administration.

Accomplishments 1974:

The staff supported by this activity continued to provide administrative management, financial management, program guidance and supportive services to the Institute's staff in the furtherance of the Institute's program to meet its goal.

* Excludes 1973 appropriation restorations.

National Institutes of Health

National Institute of Dental Research

Program Purpose and Accomplishments

Activity: Caries. (Public Health Service Act, Title IV, Part C)
Title IV, Part C)

1974			1975	
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
34	$9,102,000	Indefinite	34	$8,995,000

Purpose: In 1971, additional funds were authorized to develop the National Caries Program (NCP), a highly organized research and development effort intended to develop methods to eliminate caries as a major health problem.

Explanation: The programs of this activity are carried out by support of research grants, research contracts, graduate training grants, fellowships, research career awards, and direct operations.

Accomplishments in 1974: The general operating plan of the National Caries Program embraces four major objectives or strategies: (1) To Combat the Microbial Agent--Currently, research is concentrated on exposed surface root caries; however, research on caries of root surfaces is expanding. Dentists and oral health scientists have been aware that as teeth last longer caries of the root surface, usually associated with periodontal disease, is more frequently observed. The prevalence of this form of caries is being studied. (2) To Increase the Resistance of the Tooth--Clinical trials are being conducted on the efficacy and mechanism of different topical fluoride treatments, and the analysis of the fluoride content of enamel samples. Polymer films also appear promising in protecting the tooth surface, particularly in the pit and fissure areas. Longitudinal studies are being conducted under conditions resembling possible eventual public health use of these agents. (3) To Modify the Diet--New sweeteners are being investigated; new formulae and processes are being developed to lower the sucrose content of high-sucrose foods; an evaluation is being made of food characteristics that magnify the cariogenicity of snacks; and dietary additives are being developed to make sucrose less cariogenic in foods. (4) To Develop Methods to Improve Delivery and Acceptance of Caries Prevention Technics--Currently, studies are in progress to evaluate the benefit, cost, and acceptance of specific preventive treatment regimens in school children. Educational programs to encourage greater concern for tooth care are included in the protocols.

Approximately 58 research grants, 6 career awards, 26 fellowships, one training grant, and 40 research and development contracts will be supported in 1974.

Objectives for 1975: Research will continue within the broad framework of the four major program objectives. The most promising progress to date has been the areas of (1) combating the microbiologic agent by chemotherapy and (2) increasing tooth resistance, primarily with new topical fluorides and adhesive tooth sealants.

Approximately 53 research grants, 6 career awards, 26 fellowships, one training grant and 40 research and development contracts will be supported in 1975.

National Institutes of Health

National Institute of Dental Research

Program Purpose and Accomplishments

Activity: Periodontal and Soft Tissue Diseases. (Public Health Service Title IV, Part C)

1974			1975	
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
--	$7,648,000	Indefinite	--	$7,281,000

Purpose: The ultimate mission of the Periodontal and Soft Tissue Diseases Program is to develop new knowledge which may lead to the prevention and eradication of these diseases.

Explanation: The programs of this activity are carried out by support of research grants, research contracts, graduate training grants, fellowships, and research career awards.

Accomplishments in 1974: The major research efforts in periodontal diseases involved studies on pathogenesis and pathology with emphasis on the nature of the inflammatory response and the mechanisms of tissue destruction. It is becoming clear that different forms of periodontal disease may be caused by different bacteria. New information on mechanisms of tissue destruction that may operate in periodontal disease have provided evidence that the net loss of connective tissues observed is probably the result of depressed formation as well as enhanced degradation. Emerging evidence indicates that the inflammatory process offers mechanisms which bring about both of these effects. Efforts to develop suitable animal models for periodontal disease studies have been encouraging.

NIDR and the National Cancer Institute now have an agreement to cooperate in stimulating research in this important area. Recent significant advances in viral immunology may provide new approaches to the treatment of herpes simplex virus infection and may offer clues for the development of an effective vaccine.

Approximately 74 research grants, 12 career awards, 76 fellowships, 16 training grants, and 4 research and development contracts will be supported in 1974.

Objectives for 1975: Periodontal projects will include specific studies aimed at plaque control. Research will focus on the development of better diagnostic methods for herpes simplex virus infections and on the search for suitable treatment methods for this disease. In addition, research efforts will continue on the virology and immunology of this disease toward the development of a vaccine. Efforts will be made to conduct neoplastic diseases research with the medical community and the National Cancer Institute, particularly the regional cancer centers.

Approximately 71 research grants, 12 career awards, 82 fellowships, 16 training grants, and 4 research and development contracts will be supported in 1975.

National Institutes of Health

National Institute of Dental Research

Program Purpose and Accomplishments

Activity: Restorative Materials. (Public Health Service Act, Title IV, Part C)

1974			1975	
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
--	$2,892,000	Indefinite	--	$2,767,000

Purpose: The principal objectives of the Restorative Materials Program are to provide better dental care by fostering the development of improved materials and methods to restore lost oral tissues to normal form and function.

Explanation: The programs of this activity are carried out by support of research grants, research contracts, graduate training grants, fellowships, and research career awards.

Accomplishments in 1974: About 25 percent of the total funds in FY 1974 was expended for research to improve or develop new filling materials, about 25 percent was spent to continue projects dealing with adhesives, about 20 percent of the funds was spent on implant investigations, and 20 percent was provided for studies on maxillofacial prostheses.

Targeted efforts by contracts involving the study of marine animal adhesives have been concluded with the partial analysis of the proteinaceous cement secretions of barnacles and mussels, and preliminary characterization of the material.

Approximately 30 research grants, 4 career awards, 4 fellowships, 9 training grant, and 10 research and development contracts will be supported in 1974.

Objectives for 1975: Efforts will be continued to improve amalgams, composite resins, and other filling and adhesive materials; to evaluate different materials and designs for implants, and to develop materials to be used as artificial skin in maxillofacial prostheses.

Approximately 28 research grants, 4 career awards, 4 fellowships, 9 training grant, and 10 research and development contracts will be supported in 1975.

National Institutes of Health

National Institute of Dental Research

Program Purpose and Accomplishments

Activity: Craniofacial Anomalies (Public Health Service Act Title IV, Part C)

1974		1975		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
--	$6,180,000	Indefinite	--	$6,099,000

Purpose: Currently the cleft lip/cleft palate research of the Institute is focused on improvement and extension of treatment and understanding of the basic mechanisms as an aim toward prevention of such developmental aberrations in man.

Explanation: The programs of this activity are carried out by support of research grants, research contracts, graduate training grants, fellowships, and research career awards.

Accomplishments in 1974: Genetic-epidemiological studies are in progress to develop basis for cleft lip/palate. The studies will establish recurrence risks by (a) type of cleft, (b) severity of cleft, and (c) sex of the affected.

A more precise understanding of the roles of environment and genetics in developing the final form and function of oral-facial structures has been reached. It is now believed that the potential for modifying the growth and alignment of teeth and jaws is greater than was thought to be true earlier.

Approximately 52 research grants, 6 career awards, 45 fellowships, 11 training grants, one specialized research center, and 2 research and development contracts will be supported in 1974.

Objectives for 1975: The concept of Craniofacial Anomalies centers to achieve a cohesive effort in investigations of all congenital craniofacial anomalies will be under exploration. This is timely because of the recent breakthrough in surgical procedures of severe craniofacial deformities and the achievements of the interdisciplinary research within the cleft palate centers.

Approximately 50 research grants, 6 career awards, 53 fellowships, 11 training grants, one specialized research center, and 2 research and development contracts will be supported in 1975.

National Institutes of Health

National Institute of Dental Research

Program Purpose and Accomplishments

Activity: Pain Control and Behavioral Studies. (Public Health Service Act, Title IV, Part C)

1974			1975	
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
--	$998,000	Indefinite	--	$966,000

Purpose: The pain control activity represents the major portion of the program and deals with continuing efforts to increase knowledge concerning the nature, etiology, pathophysiology, diagnosis and treatment of the major pain problems associated with the oral-facial region. The behavioral studies component of the program encompassed efforts to achieve greater utilization of behavioral sciences knowledge in the understanding and alleviation of a variety of dental and oral problems.

Explanation: The programs of this activity are carried out by support of research grants, research contracts, graduate training grants, fellowships, and research career awards.

Accomplishments in 1974: During the past year, significant progress has been made in one type of facial pain known as the myofacial pain dysfunction syndrome (MPD) utilizing a combination of behavioral and pharmacologic approaches that has resulted in an 80% success rate. Other studies have focused on increasing the safety of nitrous oxide analgesia by an intensive investigation of its cardiovasular effects at various nitrous oxide-oxygen combinations. Progress has been reported in more basic investigations studying the ways in which stimuli from the trigeminal nerve and the tooth pulp are processed in the brain.

A comprehensive review is underway of the fear and anxiety syndrome responsible for avoidance by millions of essential dental treatment and a workshop is planned for the near future to identify new approaches toward a solution of this avoidance phenomenon.

Approximately 12 research grants, 5 career awards, 11 fellowships, 6 training grants, and one research and development contract will be supported in 1974.

Objectives for 1975: Efforts will continue to develop as many aspects of complex and multifaceted pain problem as possible. High priority will continue to be given to the development of multidisciplinary and interdisciplinary pain centers in which major oral-facial pain problems can be studied at both basic and clinical levels.

Approximately 11 research grants, 5 career awards, 15 fellowships, 6 training grants, and one research and development contract will be supported in 1975.

National Institutes of Health

National Institute of Dental Research

Program Purpose and Accomplishments

Activity: Dental Research Institutes. (Public Health Service Act, Title IV, Part C)

1974			1975	
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
--	$6,850,000	Indefinite	--	$7,200,000

Purpose: The underlying idea was to plan and develop Institutes or Centers which would bring together all of the appropriate resources of the parent universities and focus these resources upon the problems of oral health in an ideal research and training environment.

Explanation: The programs of this activity are carried out by support of research grants.

Accomplishments in 1974: The research programs of the Institutes have reached a greater degree of maturation and stabilization. Young investigators from outside dental research have developed within dental research center environments to the point of recognition as established investigators. Students are being attracted in increasing numbers to dental research institutes as the quality of institute research becomes known. Strong collaborative research programs have been developed between the Centers' investigators and other investigators at the local, regional, national, and international level. Some new approaches have been initiated to promote more interaction between the Centers and dental schools.

Objectives for 1975: This special activity is intended to achieve the most from existing dental research capability and also to develop new manpower resources by challenging scientists from medical, engineering, and graduate schools, as well as other university components. Institutes are expected to build on and extend existing institutional research strengths; provide for participation of multiple disciplines, and facilitate collaboration of a wide range of biological, physical, and social sciences in the study of oral health problems in relationships to the program objectives of the NIDR. Interaction with the educational programs of the parent university is encouraged by having an appreciable component of Institute research staff serve as active members of the academic departments representing their fields of competence. Although each Institute requires a permanent staff, participation by other scientist on a temporary or part-time basis is strongly encouraged. Institutes are also encouraged to establish mutally beneficial relationships with other regional resources including educational and research institutions, hospitals, computer facilities, MEDLARS regional centers, and primate centers.

National Institutes of Health

National Institute of Dental Research

Program Purpose and Accomplishments

Activity: Intramural Laboratory and Clinical Research. (Public Health Service Title IV, Part C)

1974			1975	
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
165	$7,282,000	Indefinite	165	$7,596,000

Purpose: The laboratory and clinical research studies of the Institute are concerned with the causes, treatment, control, and prevention of diseases and disorders of the oral cavity and facial region, e.g. dental caries, periodontal disease, oral-facial birth defects, and oral soft tissue diseases.

Explanation: Treatment, control, and prevention of oral disorders and diseases are explored through basic and applied research, both in the laboratory and clinical facilities of NIDR.

Accomplishments in 1974: Notable progress has been made in the systematic exploration of host factors in the development of periodontal disease. These immunological mechanisms dictate the host's response to the noxious agent (dental plaque), which is presumed to be responsible for the genesis of periodontal tissue destruction. No periodontal involvement in the typical variety of chronic periodontitis, occurs in a mouth free of dental plaque, information regarding the host's reaction to the plaque seems very likely to provide possible routes for preventive measures.

Research into the factors controlling infections by herpes simplex virus have been expanded. Clinical research has also continued to be rewarding in the area of salivary gland function. Basic research findings concerning the mechanism of synthesis and aggregation of the fibrous protein collagen (the predominant supporting matrix of bones and teeth), are now being extended to levels of clinical application.

Objectives in 1975: The NIDR plans to expand research efforts in the general area of immunological mechanisms. These mechanisms determine the susceptibility of the individual to infection and disease. A continuing focus on plaque is essential to understanding both dental caries and periodontal disease. A Neurophysiology and Anesthesiology Program has been established to provide a primary setting for execution of much needed basic and clinical research in problems of oral and facial pain. The primary interest in disordered facial and oral development remains that of determining mechanisms responsible for clefting of the lip and/or palate in man (a birth defect occurring in approximately 1 out of 700 live births in the United States). It is from these inquiries that potential preventive and/or therapeutic technics may make themselves evident.

National Institutes of Health

National Institute of Dental Research

Program Purpose and Accomplishments

Activity: Research Management and Program Services. (Public Health Service Title IV, Part C)

1974			1975	
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
69	$3,003,000	Indefinite	69	$3,055,000

Purpose: The Institute Director and his immediate staff are responsible for providing leadership in the field of dental research and related higher education and providing leadership in scientific investigations and manpower training.

Explanation: This activity funds: (1) the Director and his immediate staff concerned with administrative management, financial management, program planning and evaluation, and computer processing services, (2) the scientific and administrative staff responsible for grant and contract programming, review and administration.

Accomplishments in 1974: The staff supported by this activity continued to provide administrative management, financial management, program guidance and supportive services to the Institute's staff, in the furtherance of the Institute's program to meet its goals.

Objectives for 1975: In 1975 this activity will continue to provide for the overall administration, direction, and coordination of the Institute's programs.

Wednesday, March 27, 1974.

NATIONAL INSTITUTE OF ARTHRITIS, METABOLISM, AND DIGESTIVE DISEASES

WITNESSES

DR. ROBERT S. STONE, DIRECTOR, NATIONAL INSTITUTES OF HEALTH

DR. DeWITT STETTEN, JR., DEPUTY DIRECTOR FOR SCIENCE, NATIONAL INSTITUTES OF HEALTH

DR. R. W. LAMONT-HAVERS, DEPUTY DIRECTOR, NATIONAL INSTITUTE OF ARTHRITIS, METABOLISM, AND DIGESTIVE DISEASES

DR. BENJAMIN T. BURTON, ASSOCIATE DIRECTOR FOR PROGRAM ANALYSIS AND SCIENTIFIC COMMUNICATION, NATIONAL INSTITUTE OF ARTHRITIS, METABOLISM, AND DIGESTIVE DISEASES

F. L. MILLS, EXECUTIVE OFFICER, NATIONAL INSTITUTE OF ARTHRITIS, METABOLISM, AND DIGESTIVE DISEASES

DONALD F. CYPHERS, FINANCIAL MANAGEMENT OFFICER, NATIONAL INSTITUTE OF ARTHRITIS, METABOLISM, AND DIGESTIVE DISEASES

LEON M. SCHWARTZ, ASSOCIATE DIRECTOR FOR ADMINISTRATION, NATIONAL INSTITUTES OF HEALTH

LELAND B. MAY, ACTING DIRECTOR OF FINANCIAL MANAGEMENT, NATIONAL INSTITUTES OF HEALTH

CHARLES MILLER, DEPUTY ASSISTANT SECRETARY, BUDGET

Object Classification (in thousands of dollars)

Identification code 09-25-0884-0-1-651		1973 actual	1974 est.	1975 est.
	Direct obligations:			
	Personnel compensation:			
11.1	Permanent positions	9,955	10,701	10,679
11.3	Positions other than permanent	462	516	564
11.5	Other personnel compensation	49	55	58
	Total personnel compensation	10,466	11,272	11,301
12.1	Personnel benefits: Civilian	1,206	1,269	1,267
21.0	Travel and transportation of persons	251	250	250
22.0	Transportation of things	56	56	56
23.0	Rent, communications, and utilities	351	400	450
24.0	Printing and reproduction	158	160	160
25.0	Other services	16,984	19,472	21,519
26.0	Supplies and materials	1,635	1,851	1,853
31.0	Equipment	754	750	850
41.0	Grants, subsidies, and contributions	110,967	142,001	115,265
	Subtotal	142,828	177,481	152,971
95.0	Quarters and subsistence charges	−10	−10	−10
	Total direct obligations	142,818	177,471	152,961
	Reimbursable obligations:			
41.0	Grants, subsidies, and contributions	20		
99.0	Total obligations	142,838	177,471	152,961

Personnel Summary

	1973 actual	1974 est.	1975 est.
Total number of permanent positions	592	559	557
Full-time equivalent of other positions	46	51	55
Average paid employment	619	615	610
Average GS grade	8.5	8.6	8.6
Average GS salary	$14,260	$15,138	$15,473
Average salary of ungraded positions	$11,138	$12,018	$12,253

Program and Financing (in thousands of dollars)

	Identification code 09-25-0884-0-1-651	1973 actual	1974 est.	1975 est.
	Program by activities:			
	Direct program:			
	1. Arthritis, orthopedics, and skin diseases research	21,862	25,732	22,301
	2. Diabetes, endocrinology, and metabolism research	45,302	57,630	46,517
	3. Digestive diseases and nutrition research	21,990	33,839	27,098
	4. Kidney disease research	17,443	20,215	17,271
	5. Blood diseases research	10,308	11,734	10,553
	6. Intramural laboratory and clinical research	20,289	22,561	23,313
	7. Research management and program services	4,916	5,760	5,908
	Total direct program	142,110	177,471	152,961
	Reimbursable program:			
	3. Digestive diseases and nutrition research	20		
	Total program costs, funded[1]	142,130	177,471	152,961
	Change in selected resources (undelivered orders)	708		
10	Total obligations	142,838	177,471	152,961
	Financing:			
11	Receipts and reimbursements from: Federal funds	−20		
25	Unobligated balance lapsing	−24,530		
	Unobligated balance restored (−)		24,530	
	Budget authority	**167,348**	**152,941**	**152,961**
	Budget authority:			
40	Appropriation	167,316	159,447	152,961
	Withheld from obligation and expenditure (Public Law 93-192)		6,486	
41	Transfer to other accounts (−)		−20	
42	Transferred from other accounts	32		
43	**Appropriation (adjusted)**	**167,348**	**152,941**	**152,961**
	Relation of obligations to outlays:			
71	Obligations incurred, net	142,818	177,471	152,961
72	Obligated balance, start of year	77,100	71,256	77,213
74	Obligated balance, end of year	−71,256	−77,213	−41,317
77	Adjustments in expired accounts	866		
90	Outlays	149,528	171,514	188,857

[1] **Includes capital outlay as follows: 1973, $754 thousand; 1974, $750 thousand; 1975, $850 thousand.**

NOTES

Includes $302 thousand in 1975 for activities previously financed from:	*1973*	*1974*
National Institute of General Medical Sciences	256	256
Departmental Management	2	2

Excludes $63 thousand in 1975 for activities transferred to: Office of Assistant Secretary for Health. Comparable amounts for 1973 ($63 thousand) and 1974 ($63 thousand) are included above.

Excludes $20 thousand in 1974 and 1975 for activities transferred to Departmental Management. Comparable amount for 1973 ($32 thousand) is included above.

Mr. Flood. We now have the National Institute of Arthritis, Metabolism, and Digestive Diseases.

WITNESS INTRODUCTION

The presentation is to be made by Dr. R. W. Lamont-Havers, Deputy Director of the National Institute of Arthritis, Metabolism, and Digestive Diseases.

You have a biographical sketch, which will be included in the record.

[The information follows:]

Department of Health, Education, and Welfare

National Institute of Arthritis, Metabolism, and Digestive Diseases

Biographical Sketch

Name: Dr. Ronald W. Lamont-Havers.

Position: Deputy Director, National Institute of Arthritis, Metabolism, and Digestive Diseases (NIAMDD).

Birthplace and date: Wymondham, Norfolk, England, March 6, 1920.

Education: B.A., 1942, University of British Columbia; M.D., 1946, University of Toronto.

Experience: Deputy Director, NIAMDD, 1972–president; Assistant Director for Extramural Research and Training, NIH, 1968–1972; Associate Director for Extramural Programs, NIAMDD, 1964–1968; Instructor in Medicine, College of Physicians and Surgeons, Columbia University, Columbia Presbyterian Hospital, 1955–1964; Associate Medical Director—Medical Director, Arthritis and Rheumatism Foundation, 1955–1964; Medical Director, Canadian Arthritis and Rheumatism Society, British Columbia Division (also private practice and consulting positions), 1953–1955; Fellow of the Canadian Arthritis and Rheumatism Society, Columbia Presbyterian Hospital, College of Physicians and Surgeons, Columbia University, 1951–1953; Resident, Queen Mary Veteran's Hospital (Montreal), 1949–1951; Associate Medical Director Student Health Service, University of British Columbia, 1948–1949; House Staff and Residency Training, Vancouver General Hospital (Canada), 1946–1948.

Association memberships: Arthritis Foundation (Board of Directors and Governing Member, 1966–present, Medical Advisory Committee, 1971); Dermatology Foundation (Medical Advisory Committee and Executive Committee, 1967–present); American Rheumatism Association; New York Rheumatism Association (President 1961); Canadian Rheumatism Societies; American Rheumatism Association of Metropolitan Washington (Board of Directors 1955–present, Medical Advisory Committee, 1969–present, Medical Advisory Committee, 1969–present); D.C. Rheumatism Society (President 1971); Affiliate Member, American Gastroenterological Association.

Special awards, citations or publications: Consultant, Code Authority of the National Association of Broadcasters, 1962 to present; Consultant to Grayson Foundation, Inc., Lexington, Ky., 1965 to present; Fellow of the Royal College of Physicians (Canada), Internal Medicine, 1952; Diploma, Internal Medicine, McGill University, 1953; Member, Alpha Omega Alpha, Honorary Medical Society; Editor, Bulletin of Rheumatic Diseases, 1964–1966; Golden Pen Award, Editorial Board, Journal of the American Physical Therapy Association, 1965; DHEW Superior Service Award, 1973.

Dr. Lamont Havers is the author of over 40 publications on arthritis, rheumatic diseases, rehabilitation, support and administration of biomedical research, et cetera.

Dr. Lamont-Havers. I would like to introduce Mr. Mills, our Executive Officer; on his left, Mr. Don Cyphers, the Budget Officer; and behind me, Dr. Benjamin Burton, who is the Associate Director of the Institute.

Mr. Flood. You have a prepared statement.

Dr. LAMONT-HAVERS. I would like very much to read that, and then lead to questions from that.

Mr. FLOOD. Suppose you do that.

OSTEOPOROSIS

Dr. LAMONT-HAVERS. I would like to mention the fact that Dr. Whedon, the Director of the Institute, wished me to express his apology and deep regret that he would not be able to be present today to testify on behalf of the Institute. Dr. Whedon had confidently expected to testify. The unexpected speedup of the hearings, however, made it impossible for him to return from Israel, where the opportunity had presented itself to initiate a long-planned clinical investigation project related to osteoporosis.

This is a project which could have great significance to millions of Americans, but which could not have been carried out in this country.

Mr. FLOOD. What is the nature of that disease?

Dr. LAMONT-HAVERS. Osteoporosis is a disease, extremely common as we get older, of thinning of the bones, and leads to fractures and collapse of vertebrae, primarily, which is a terrible problem in older people.

Mr. FLOOD. Does this result in many bone fractures?

Dr. LAMONT-HAVERS. Yes, sir, mostly hip fractures and collapsed vertebrae.

It is also, by the way, a problem with the astronauts, and Dr. Whedon has been studying them, also.

Mr. FLOOD. All right, you may proceed.

Dr. LAMONT-HAVERS. Dr. Whedon, by the way, has always felt it one of his most important and more congenial duties to appear before this committee to report——

Mr. FLOOD. A man of very sound judgment.

Dr. LAMONT-HAVERS. Yes, sir, on our progress in health research and to outline future efforts of our programs. This would have been his 13th year of appearances before you. He is especially mindful of the role which this committee has played in stimulating biomedical research.

OPENING STATEMENT

Our own research areas include, among others, arthritis and connective tissue diseases, diabetes, and other metabolic disorders, digestive diseases and nutrition, diseases of the kidneys and urinary tract, diseases of the blood, bone, and skin, and the field of orthopedic surgery. In order to present a broader description than is possible in this brief presentation of the background, progress and directions of our research, we have prepared special reports in a number of major fields, which I am submitting hereby to the committee.

[The reports follow:]

ARTHRITIS, RHEUMATIC DISEASES, AND RELATED DISORDERS

More than 18 million people in the United States suffer from arthritis, rheumatic diseases, and related disorders, at an annual cost to the nation of about $4 billion. Rheumatoid arthritis, the most severely crippling form of the disorder, afflicts about 5 million Americans. More than half of all people between the ages of 55 and 64 show evidence of degenerative joint disease, such as osteoarthritis, which is the most prevalent form. Despite these figures, important advances against these diseases are apparent at both basic and applied levels of research, largely as a result of extensive biomedical investigations conducted and supported by the National Institute of Arthritis, Metabolism, and Digestive Diseases.

Obligations for Programs in Arthritis

	1971	1972	1973	1974 estimate	1975 estimate
National Institutes of Health:					
National Institute of Arthritis, Metabolism, & Digestive Diseases...	$12,351,000	$14,374,000	$13,808,000	$13,941,000	$13,860,000

NATIONAL INSTITUTES OF HEALTH

National Institute of Arthritis, Metabolism, and Digestive Diseases

Arthritis is the oldest known chronic disease and the greatest crippler in the United States today. Actually, a number of diseases are included under the term "arthritis" - distinct disorders afflicting joints with inflammation and eventually with degenerative changes, and, in some cases the adjoining musculature as well. There are about a hundred of these rheumatic disease entities, of which more than a dozen represent serious public health problems. These include rheumatoid arthritis, degenerative joint diseases, such as osteoarthritis, connective tissue disorders such as systemic lupus erythematosus, and arthritis associated with metabolic abnormalities such as gout.

Each year, rheumatic diseases cause unemployment equivalent to the loss of 500,000 people. The cost to the government of disability payments to individuals crippled by arthritis during this decade will be more than $1 billion. No price can be set on the suffering these afflictions impose on people.

Investigators and grantees of the National Institute of Arthritis, Metabolism, and Digestive Diseases (NIAMDD) are conducting basic and clinical research on the processes of arthritic inflammation and tissue destruction and the immunologic mechanisms which may be related. These studies are fundamental to understanding and treatment of arthritis and to perfection of such procedures as total hip or knee replacement.

RHEUMATOID ARTHRITIS

Intensive efforts continue toward discovery of the causes of rheumatoid arthritis, which afflicts about one-third of those who present themselves for treatment of rheumatic disease. No permanent cure has yet been found for this disease, which often leads to severe disability. Research is also being concentrated on the search for effective drugs. Although several infectious agents have been found in close association with tissues inflamed by rheumatoid arthritis, none has yet been identified as a cause of the disease. Many investigators are convinced that the disorder is the result of chronic inflammation, caused by an abnormal immune (protective) reaction, which may in turn be the result of an initial infection or an autoimmune reaction (a misdirected attack by the body's defense systems on its own tissue), or some combination of these.

Research on the Mechanisms of Immunity and Infectious Agents

Studies at the Mayo Foundation, Rochester, Minnesota, by Dr. Frederic C. McDuffie and his associates have indicated that the chronic inflammation observed in tissues of patients with a disseminated form of rheumatoid arthritis is accompanied by increased immune reactions (with enhanced immunoglobulin levels and rheumatoid factor levels in the blood) and by a drop in serum complement values. Numerous studies in recent years have pointed to the involvement of complement, a protein component of blood, in the body's immunological responses, and to a deficiency of complement in the synovial fluid of some rheumatoid arthritis patients. In the 16 patients studied, complement values were lowest during exacerbations of the joint disease or development of extra-articular complications. The low levels of complement during enhanced immune reactions suggests the utilization of complement during the formation of immune complexes. The concurrence of low levels of complement with exacerbations of rheumatoid arthritis suggests that complement-fixing immune complexes are actively involved in those events.

Another important area of investigation involves the association of prostaglandins, hormone-like substances that act locally in many tissues of the body that are inflamed. Most prostaglandins which have been studied have been implicated in triggering tissue inflammations. One particular member of the group, however, prostaglandin E_1, has now been shown to be capable of suppressing arthritis-related inflammation. Dr. Gerald Weissman, an Institute grantee, and associates at the New York University School of Medicine, have recently demonstrated that large doses of prostaglandin E_1 can suppress the inflammation and tissue damage in rats in whom experimental arthritis is induced. This team also developed evidence that the prostaglandins probably switch off inflammation by inhibiting the release of potent tissue-dissolving enzymes (lysozymes) from white blood cells. Research into the role of prostaglandins in rheumatoid arthritis is continuing.

At the NIH Clinical Center, Institute researchers are studying patients with juvenile rheumatoid arthritis in the attempt to isolate infectious agents, such as viruses. Investigators believe such an agent may be more easily found in patients with recent active joint disease, as in some of these cases, than in the chronic form of the disease.

Despite occasional reports associating particular organisms with rheumatoid arthritis, no single organism has been shown to be an important or specific cause of the disease. Even so, a number of agents such as rubella virus, diphtheroid bacteria, bacterial L-forms, virus-like bodies, and mycoplasma have been isolated from rheumatoid tissues, and evidence of increased immunological activity in the damaged tissues often accompanies this.

Institute scientists and grantees have searched for viral agents associated with rheumatoid arthritis. The investigators tested the susceptibility of cells taken from rheumatoid patients to seven different viruses, including rubella and Newcastle disease viruses. No differences were found between cells from rheumatoid arthritis patients and cells from non-rheumatoid patients. The researchers indicate that the search for infectious causes for certain rheumatoid diseases will still be actively pursued.

Therapy for Rheumatoid Arthritis

Treatment of rheumatoid arthritis varies widely, because the course and severity of the disease is so diverse. Some cases can be controlled satisfactorily with salicylate drugs (such as aspirin) and do not progress to significant joint destruction or interfere with the normal routine of the patient's life. In other cases, even progressive joint damage can be stopped or slowed down with salicylates and gold salts. Some cases are controlled with corticosteroid drugs, administered alone or in combination with aspirin or gold. Since the Institute introduced the first effective antirheumatic, synthetic corticosteroid drug, prednisone, into clinical practice more than two decades ago, it has continuously contributed to the search for more effective drug therapy.

In recent years, numerous investigators have reported beneficial results in treating severe cases of rheumatoid arthritis which cannot be checked by conventional therapies with such immunosuppressive drugs as cyclophosphamide and azathioprine. Considerable discussion now centers on use of these drugs, because of their toxic nature and untoward side effects. Investigators emphasize the need to follow certain strict guidelines for their use. These include restricting use to cases with life-threatening complications or potential for serious crippling, where other therapy has been ineffective, and where meticulous follow-up is assured.

A few patients have now been taking cyclophosphamide for more than five years under different dosage schedules, but not enough patients have used the drug this long to define potential problems of long-term administration. Azathioprine has been shown effective against rheumatoid arthritis that is unresponsive to conventional treatment but as with cyclophosphamide, toxicity can be a severe problem.

Other agents with toxic effects have also been shown to be effective, such as nitrogen mustard, methotrexate and chlorambucil. Use of nitrogen mustard is limited by the fact that it must be injected and by its toxicity. Evidence of the efficacy of methotrexate is still limited. Chlorambucil has not been tested in controlled studies, but seems promising for more extensive investigation.

Until recently, synovectomy, surgical removal of the thickening synovial tissue, was generally used only in advanced cases, but surgeons at the Clinical Center facilities have demonstrated that synovectomy at an early stage can lead to regrowth, in the same joint, of healthy tissue. Usually this procedure results in reduced inflammation in the joint, with accompanying relief from pain. Further research is needed to determine which patients are likely to benefit from synovectomy and its long-term effects of the surgery on the progression of rheumatoid arthritis.

Influence of Joint Temperature on Cartilage Degradation

Collagenase is a natural enzyme which catalyzes the destruction of collagen, the main supportive protein of cartilage and connective tissue. It has long been believed that collagenase plays a primary role in the joint destruction of rheumatoid arthritis, but solid evidence has been lacking.

An Institute grantee at Dartmouth University, Dr. Edward D. Harris, Jr., now has demonstrated in laboratory studies that human cartilage collagen fibrils normally are relatively resistant to destruction by human collagenase. The rate of collagen destruction, however, was found to be affected by changes in reaction temperature. At temperatures found within inflamed rheumatoid knee joints (34-37.6° C) collagen breakdown was four times greater than at temperatures in normal knee joints (30.5-33° C).

It is well established that treatment of inflamed joints with induced heat (such as diathermy) increases internal joint temperatures and almost invariably aggravates the inflammation. Dr. Harris' work suggests that part of the benefit from anti-inflammatory therapy in rheumatoid arthritis may be secondary to lowering the internal temperature of the affected joints, thereby decreasing the rate at which collagenase degrades cartilage collagen. His finding provides a scientifically acceptable rationale for effective local suppression of joint inflammation, particularly by intra-articular injection of potent steroid drugs.

Juvenile Rheumatoid Arthritis

Rheumatoid arthritis is similar in many ways whether it occurs in children or in adults, but there are also marked differences. Juvenile rheumatoid arthritis (JRA) affects those under the age of 16 years; it causes growth disturbances and causes more frequent occurrence of high fever and skin rash than is the case among older patients. There are also characteristic systemic and visceral disorders, and frequently an absence of rheumatoid factor in the blood. Because of these distinctions, JRA is looked upon as a separate disease entity.

Investigators at the Institute have conducted studies which indicate, however, that JRA can begin in adult life, in which case the patients are said to have "seronegative rheumatoid arthritis." This is an important distinction because the prognosis for adult patients with JRA is generally favorable; the disorder frequently subsides spontaneously with little damage and restoration of normal function of the joints.

Other investigators working under a grant from the National Institute of Allergy and Infectious Diseases analyzed the course of disease in 124 children with JRA and concluded that there are three distinct subgroups of disease patterns, suggesting that what is now referred to as JRA may be more than a single disease.

OTHER CONNECTIVE TISSUE DISORDERS

Systemic Lupus Erythematosus

Another leading connective tissue disorder in which the Institute supports research is systemic lupus erythematosus (SLE), a chronic inflammatory disease of unknown origin which may affect various organs. It affects some 50,000 new victims each year, particularly young women, generally those between 20 and 40 years of age.

Considerable evidence indicates that SLE may be a disorder of the immune mechanism of the body, and that it may be triggered by an infectious process. On the other hand, the disease sometimes appears in connection with hypersensitivity to certain drugs, and Institute researchers are studying this phenomenon. Investigators at the Clinical Center are also studying the value of the immunosuppressive drugs cyclophosphamide and azathioprine in treating certain complications of SLE.

The presence of circulating antibodies to nuclear components like DNA is a characteristic of active stages of SLE. Institute grantee Dr. Nicholas M. Kredich and his associates at the Duke University Medical Center, have developed a rapid and reliable method for directly measuring antibodies to DNA in the blood of SLE patients. This may be useful in predicting the emergence of complications, such as kidney disease, several days to several weeks before they occur. They suggest that this technique may lead to improved diagnosis and management of SLE patients.

Osteoarthritis and Collagen Metabolism

Degenerative joint disease (osteoarthritis) is extremely common. It is progressive, noninflammatory, and is characterized by deterioration of the smooth cartilage, which acts like the surface of a bearing in the joint, and formation of new bone beneath the cartilage and at the margins of the joint. The disease appears to be a part of the aging process and is most common in the elderly but is also seen in younger people. Research into the mechanisms underlying osteoarthritis offers hope that more definitive approaches to treatment can be discovered.

Considerable interest centers upon the structure and functions of collagen, the body's most abundant protein and structural component which is the essential ingredient in connective tissues, including bones, skin, teeth and blood vessels.

Recently, two grantees of the Institute, Dr. Marcel Nimni and Dr. Kalindi Desmukh of the University of Southern California School of Medicine, presented evidence that the particular molecular structure of cartilage collagen explains the mechanical strength and integrity of joint cartilage. Comparison of collagens from normal and osteoarthritic joint cartilage showed that the diseased cartilage synthesizes a collagen structural difference from normal joint cartilage. The investigators suggest that the different features of the two types of collagen may account for some of the functional defects of osteoarthritic cartilage.

GOUT

Gout, which affects more than 500,000 Americans is a hereditary disorder of purine metabolism, in which uric acid, a breakdown product of purines, accumulates or is produced in excess by the body, and its salt (sodium urate) is deposited under the skin, in the urinary tract, or in and around the joints. These salt crystals may cause excruciating pain in the joints. If the victim is not treated the deposits grow until they form distinct masses that may build up until there is permanent destruction of the joints with crippling, or impairment of kidney function.

Of the common joint disorders, gout is the most treatable, due in part to research conducted and supported by the Institute. Investigators have studied such drugs as allopurinol, which inhibit uric acid synthesis and build up in the body, and others which stimulate the renal excretion of uric acid from the body.

Recently, NIAMDD grantee Dr. J. Edwin Seegmiller and his associates at the University of California, San Diego, reported purine overproduction and gouty arthritis in some patients can be traced to increased activity of an enzyme of purine metabolism. The researchers describe this distinct abnormality as an indication that disease states may result from genetic alterations leading to increased as well as diminished enzyme function. This is in contrast to most known inborn errors of metabolism, which are based on impairment or lack of a key enzyme.

ORTHOPEDIC RESEARCH

Total replacement of the hip has proven to be one of the most successful orthopedic procedures in restoring hip mobility, even in cases where previous reconstructive surgery has failed. In recent years extensive development of surgical techniques and materials have contributed to the success of implants replacing hip, wrist and finger joints. These amount to custom replacements of both sides of the joints.

In a typical total hip replacement operation, the neck of the thigh bone is removed and a metal shaft is cemented into place as a substitute. The shaft is topped with a metal ball designed to move freely within a plastic socket that is cemented into place in the pelvic girdle. The effectiveness of such prostheses has been advanced through development of an acrylic cement, methyl methacrylate, first used by dentists to seal dentures. The cement has been widely used in total hip replacements for about two years. The operation restores about 90 percent of the mobility of a normal hip and means the difference between disability and relative freedom of movement to most patients. Experience has shown such prostheses are effective over a span of ten years. Additional experience is needed to indicate if the working life time of man-made joints extends over still longer periods, so that they may be implanted safely in middle-aged patients who require them.

Knee Joint Replacement

Methyl methacrylate has recently been employed in advanced techniques of knee joint replacement. An institute grantee, Dr. Gerald A. M. Finerman, and associates at the University of California at Los Angeles, and research teams from four other medical centers, have replaced 300 knee joints severely damaged by osteoarthritis or rheumatoid arthritis. Results are encouraging.

Two hundred patients have received the "concentric total knee prosthesis," and 100 have received a different type, a "geometric" prosthesis. The latter conforms to geometric lines of force, not an anatomic outline. Total knee replacement in aged patients has provided, in almost every instance, relief of pain and sufficient function to permit basic daily activities previously denied.

Another Institute grantee, Dr. Clement B. Sledge at Harvard Medical School, is working with a team to develop an artificial knee that nearly duplicates the knee joint both anatomically and mechanically. The prosthesis, called the "Ewald knee" after Dr. Frederick Ewald, is being tested for wear-resistance in a knee-bending apparatus before implantation in patients.

Through studies such as these, the outlook for replacement of joints in the treatment of arthritic conditions is being rapidly improved. Within the next few years, it is expected prostheses with increased wear characteristics and cements which are completely and indefinitely compatible with human bone will be possible.

OUTLOOK

The findings reported here reflect the commitment of the Institute and the progress in the fight against arthritis, rheumatic diseases, and related disorders. The studies mentioned are examples of more than 150 ongoing research efforts conducted or supported by the Institute. These efforts are continually adding to a valuable fund of basic knowledge, as well as improving treatment and control of arthritic and rheumatic diseases.

COOLEY'S ANEMIA AND OTHER BLOOD DISORDERS

Studies in the field of hematology (the study of blood) are essential to provide a better insight into blood processes and mechanisms in health and disease and the genetic basis of inherited blood disorders such as Cooley's anemia. It is estimated that there are more than 1,000,000 persons in the United States who suffer from disabling or killing disorders of the blood, including the anemias and bleeding disorders.

Blood disorders and anemias are conducted and supported by the National Institute of Arthritis, Metabolism, and Digestive Diseases (NIAMDD). The Institute's program, with an estimated 1975 budget of $11,434,000 includes such disease entities as the various hemoglobinopathies (genetically transmitted abnormalities of the hemoglobin molecule causing aberrations in its physical and chemical characteristics), chronic hemolytic anemias (such as thalassemia major, better known as Cooley's Anemia), blood clotting disorders ("bleeding" diseases such as hemophilia), Rh incompatibility, thrombocytopenic purpura, and anemias of other origin. The National Heart and Lung Institute shares the responsiblity for Cooley's anemia research.

Obligations for Programs in Cooley's Anemia

	1973	1974 Estimate	1975 Estimate
National Institutes of Health:			
National Institute of Arthritis, Metabolism, & Digestive Diseases			
Cooley's anemia	992,000	$1,300,000	$1,300,000
National Heart and Lung Institute:			
Cooley's anemia	1,121,000	1,206,000	1,325,000
TOTAL	2,113,000	2,506,000	2,625,000

NATIONAL INSTITUTES OF HEALTH

National Institute of Arthritis, Metabolism, and Digestive Diseases

A steady advance has been made in our knowledge of these diseases, much of it during the past decade. Diagnostic techniques in the blood diseases have become more precise, and prompt and accurate diagnosis is frequently the key to successful treatment. Institute-supported research has contributed much to knowledge of the molecular structure of hemoglobin, the key substance in red blood cells which carries oxygen from lungs to tissues, and of the disordered sequence of amino acid building blocks in abnormal hemoglobins.

Substantial advances have been made recently in the physical chemistry of blood-clotting mechanisms and in the understanding of bleeding disorders.

Through research in its Bethesda laboratories and clinics, and througn numerous grants to scientists at research centers across the country, the National Institute of Arthritis, Metabolism, and Digestive Diseases (NIAMDD) is investigating many blood disorders. As blood is so complex, any new discovery about it will open up other possibilities of biomedical investigation in related fields as well. This past year, investigations have contributed many important research findings.

Cooley's Anemia

New initiatives and research are forthcoming in the area of Cooley's anemia following passage of the National Cooley's Anemia Control Act, which provides for expanded programs of research, diagnosis, prevention and treatment of this disorder. The main responsibility for conducting research in Cooley's anemia rests with the NIAMDD. Under the provisions of the National Heart, Blood Vessel, Lung and Blood Act of 1972, however, a comprehensive national plan for the future research needs in Cooley's anemia will be included in the NHLI's report required under that Act.

Cooley's anemia is an inherited blood disorder which occurs primarily in persons of Mediterranean ancestry. In the United States most of the victims are of Italian, Greek, Turkish, French or North African descent, although the disease is not limited to these groups.

As in many genetic blood disorders, those who inherit the trait for the disease from only one parent will become "carriers" (who can pass on the trait to their own offspring) and are usually free of symptoms; those who inherit the gene from both parents have the overt disease. This severe form of the disease occurs in one fourth of the children of parents who both carry the trait. Cooley's anemia is characterized by the production of abnormally thin red blood cells with abnormal mechanical fragility and by a profound anemia which appears soon after birth, with severe effects including enlarged spleen and liver and grossly active bone marrow which may produce thickening of facial bones.

No cure is known, and the only effective treatment is administration of blood transfusions, usually once a month, but sometimes more frequently, to alleviate the constantly recurring anemia. A serious complication is a progressive overload of iron in the body resulting from frequent transfusions. There are agents with limited effectiveness in removing the excess iron, but those now available are too toxic for general use. Carriers generally enjoy normal health and life span. The prevalence is not really known. The best available estimate is that about 200,000 persons in the country carry the trait. There is no national estimate of the number of cases of clinical disease, but it is reported that there are 1,000 cases known in New York City.

Diagnosis is simple in those who have clinical disease, but definitive diagnosis in those who only carry the trait is much more difficult and requires relatively sophisticated hematologic tests. Experts have indicated that there is as yet no simple and reliable screening test, although progress in this area is being made.

Cooley's Anemia Screening Test

The National Heart and Lung Institute has assumed responsiblity for administration and funding of a program to develop a screening test both "effective and inexpensive". The specifications of the work to be performed under the contract are being developed. It is expected that it will be possible to award a contract to begin work early in FY 1975 and that a period of approximately two years will be required for the first phase to be completed.

Iron Chelating Agent

The National Cooley's Anemia Control Act declares that "attainment of better methods of prevention, diagnosis, and treatment of Cooley's anemia deserves the highest priority". To carry out this mandate the Inter-Institute Coordinating Committee for Cooley's Anemia was organized by the National Institutes of Health. This committee felt that the development of an effective iron chelating (removing and binding) agent was one of the two areas of highest feasibility and priority; the other matter given top priority was a simple and reliable screening test. The urgency of this activity is based on the fact that the illness and deaths of patients with Cooley's anemia is due primarily to the deposit of large quantities of iron in vital organs (heart, liver and kidneys). This excess iron, as noted earlier, is a residue of multiple blood transfusions that these patients must receive in order to remain alive. Patients maintained on regular (monthly) transfusions are relatively healthy until iron deposits begin to produce symptoms of heart failure or liver failure. Several iron chelators developed in the past have proven too toxic for general use. The National Institute of Arthritis, Metabolism, and Digestive Diseases is initiating research to develop a safe, effective, iron chelating agent (preferably oral) for use in removal of iron deposits from patients suffering from iron overload, such as in Cooley's anemia.

Intramural Research

Research conducted at the National Institutes of Health on Cooley's anemia is carried out primarily in the Molecular Hematology Branch of the National Heart and Lung Institute. This program, which has recently been expanded, is exclusively involved in the clinical and laboratory study of hereditary anemias, with a primary interest in Cooley's anemia. The laboratory portion of the Branch has succeeded in synthesizing hemoglobin in a cell-free system using components isolated from human red blood cells. They have determined that the molecular defect in Cooley's anemia is carried by the messenger RNA and that the cellular defect of the thalassemic cell can be reproduced in a normal cell-free system by the addition of the isolated messenger RNA molecule from the diseased cell. They have recently developed a cell-free system in which the messenger RNA can be synthesized directly from thalassemic chromatin (i.e., thalassemic DNA). The regulation of hemoglobin gene expression in bone marrow cells grown in tissue culture is also being studied. In the newly created clinical program, patients with Cooley's anemia, sickle cell anemia, and other congenital hemolytic anemias are studied.

Blood Disorder Responds to Corticosteroids

Idiopathic thrombocytopenic purpura, or ITP, is an uncommon blood disorder characterized by easy bruising and bleeding, a deficiency of blood platelets, and a prolonged bleeding time. Institute grantee Dr. Byrd S. Leavell of the University of Virginia has shown that the immediate response of patients with ITP to corticosteroid therapy permits prediction of their response to continued steroid therapy or to surgical removal of the spleen which produces sustained remissions in 60-90% of patients with ITP.

A 25-year-study of the response to steroid drug therapy and splenectomy has indicated that the initial response to steroid therapy is a reliable indicator of prognosis. Patients with excellent responses to initial steroid therapy usually remain in complete remission. Patients whose platelet count falls after steroid therapy usually make a good to excellent response to surgery for removal of the spleen.

Sickle Cell Anemia

The National Heart and Lung Institute and components of the Health Services Administration are engaged in special targeted research, field studies, and genetic screening and counseling to combat sickle cell anemia. The NIAMDD had engaged in research and research support in sickle cell anemia prior to organization of the special program; because of its previous productivity, this research is continuing.

Sickle cell anemia is a grave, hereditary blood disorder that affects the black population almost exclusively, and is difficult to treat. Normally red blood cells, or erythrocytes, which transport oxygen throughout the body, are biconcave discs; in sickle cell anemia, under conditions of diminished oxygen tension, the contoured, biconcave disc shape changes to a crescent shape; log-jams of these abnormally shaped cells then clog capillaries, causing obstructions and blood clots and depriving local tissues or organs of their supply of blood.

Sickle Cell in Black Football Players

Institute grant-supported researcher Dr. John R. Murphy of Case Western Reserve University, Cleveland, Ohio, has shown that the sickle cell trait among black National Football League (NFL) players differs little from that of the general black U.S. population (7.7%) and, thus, is clearly no barrier to participation and excellence in one of the most rigorous and demanding of professional sports.

The sickle cell anemia trait has been detected in 6.7% of the black football players in the league, a prevalence that indicates there has not been a selective exclusion from professional football of individuals with the trait because of expected limitation in physical capabilities. Furthermore, this is an indication that there is no need for any selective exclusion from other, less physically demanding, activities. Twenty of the 26 teams in the NFL participated in the study. Blood samples were obtained from 579 black players in spring training camps. Of the players tested, 39, or 6.7% were found to have the sickle cell trait. The present study supports a recent evaluation by the National Academy of Sciences-National Research Council of the status of sickle cell trait carriers in the Armed Forces. The latter study recommended that there be no limitation on activity except for pilots and co-pilots, who may suffer sickle cell crises following exposure to low oxygen tension at high altitudes in nonpressurized planes.

Mass Screening for Sickle-Cell Anemia

Insitute grantee Dr. Michael D. Garrick of the State University of New York, Buffalo, has devised a simple, practical and inexpensive method for detecting sickle-cell disease and other hemoglobin abnormalities, which utilizes dried blood specimens on filter-paper, similar to that used in mass screening of newborn infants for phenylketonuria (PKU). This convenient and inexpensive procedure has now been adapted at a cost of only 3 cents per specimen. It permits screening of 250-500 specimens per day.

Outlook

Hematology is an integral part of the research conducted and supported by the National Institute of Arthritis, Metabolism, and Digestive Diseases. The number of Americans afflicted with the disabling and killing disorders of the blood, excluding circulatory problems, but including the anemias, and blood-clotting disorders such as hemophilia, is sufficient to justify the effort. Among Institute research goals is a definition of the specific defects in blood disorders, and enhanced knowledge of the precise steps in normal and abnormal blood clotting mechanisms, preparatory to improved diagnosis and therapy. New research should yield maximal benefits in the number of lives saved today and the deaths prevented in years to come.

CYSTIC FIBROSIS

It is estimated that one baby in every 1,400 infants is born with cystic fibrosis (CF), one of the inherited metabolic diseases. It is characterized by malfunctioning exocrine glands which secrete abnormal fluid to internal and external body surfaces, particularly to the gastrointestinal and respiratory mucosal linings and the skin.

The Department of Health, Education, and Welfare's research activities in cystic fibrosis are centered in the National Institute of Arthritis, Metabolism, and Digestive Diseases, a component of the National Institutes of Health in Bethesda, Maryland, and service activities of the Department are located in Maternal and Child Health/Bureau of Community Health Services of the Health Services Administration.

The research conducted and supported by the NIAMDD is aimed at specifically defining clinical manifestations and biochemical aberrations associated with this disease. In addition to investigations carried out in the Bethesda laboratories, the NIAMDD supports many cystic fibrosis research projects at medical centers and institutions across the country through the research grant mechanism. This combined effort has thus far uncovered several promising leads in pinpointing the molecular defect in this inherited metabolic disease.

Obligations for Programs in Cystic Fibrosis

	1971	1972	1973	1974 estimate	1975 estimate
National Institutes of Health:					
National Institute of Arthritis, Metabolism, and Digestive Diseases...	$2,637,000	$2,777,000	$2,525,000	$2,525,000	$2,680,000
Health Services Administration:					
Maternal and Child Health/Bureau of Community Health Services.	[1]	[1]	[1]	[1]	[1]
Total..................	2,637,000	2,777,000	2,525,000	2,525,000	2,680,000

[1] Obligations not identifiable.

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This basic metabolic disorder of exocrine secretion results in three principal clinical problems. The first is the production of sweat with a high salt content. Because of this defect, patients are unable to conserve salt, and the very young are at risk of developing profound dehydration or heat exhaustion in the summer, both of which may be fatal.

The second is that in CF the mucus-secreting glands of the body fail to secrete normal, clear, free-flowing fluid. Instead, they produce abnormally thick, viscous mucus which tends to obstruct the ducts or openings of the glands. When the mucus accumulates in the ducts of the pancreas, it interferes with the ability of this gland to supply digestive enzymes to the intestinal tract, thus leading to poor digestion and malabsorption of a number of nutrients. Depending on the severity of this complication, the patient may suffer from general underdevelopment, poor musculature, and retarded bone growth.

The third and most serious complication is the development of progressive, chronic lung disease. Thick mucus obstructs the smaller air passages in the lung, causing labored breathing and a chronic cough. In time, bacteria multiply in the accumulated secretions, predisposing the child to chronic bronchitis or pneumonia - a leading cause of death in these patients. The lung changes also may restrict pulmonary blood flow, leading to increased blood pressure in the lung and to consequent chronic heart strain and eventual heart failure.

State of the Research Art

Many Institute-supported research projects in CF are related to applications of existing medical knowledge to treatment, while other, more basic, studies involve the search for a specific biochemical defect or genetic abnormality responsible for the disease. Some of these projects have implications for improving tests for early diagnosis (or developing new ones), for elucidating the specific mechanism of exocrine gland dysfunctions, and for determining the nature of the molecular defect in cell components.

One important factor in the management of this disease is to establish a correct and early diagnosis prior to the development of irreversible pulmonary and pancreatic lesions. The most widely used diagnostic test, based upon an abnormally high concentration of salt in sweat, reflects one of the manifestations of exocrine gland dysfunction. A number of research projects are concerned with secretory mechanisms, including those of the sweat glands, salivary glands, and of the respiratory and gastrointestinal systems.

A disease of many disguises, cystic fibrosis offers only enigmatic clues to the disorder's basic mechanism. Yet, promising findings in fundamental research and innovative methods of diagnosis and treatment have opened up new avenues for investigation, resulting in a somewhat more optimistic outlook for patients.

New Patient Evaluation System

An indication of progress in cystic fibrosis is the increased average life span of afflicted children with the disease and the concurrent improvement in the quality of their lives. On the other hand, since a significant number of these patients now survive to childbearing age, new emphasis must be placed on the development of reliable and simple tests to detect carriers of cystic fibrosis and on initiation of active genetic counseling wherever indicated.

The questionable life expectancy of children with cystic fibrosis is an agonizing reality that physicians, parents and the patients themselves must eventually face. To assist in assessing the anticipated approximate length of survival, NIAMDD investigators in Bethesda have developed a simple, comprehensive system for objective evaluation of patients. It provides the physician with a concise summary of each patient's clinical course, and a numerical prediction of life expectancy.

A previous scoring method had been developed in 1958, before prognosis and life expectancy improved, and before the incidence of new complications resulting from the increased average age of patients.

Several studies have established the relationship of pulmonary function tests to overall severity of disease and prognosis, so the prognostic score is heavily weighted (75 out of 100 points) toward the pulmonary component. The subcategories of this section take into account results of common tests and complications, some of which have recently demonstrated prognostic significance. The remaining 25 points of the scoring method are divided among weight, activity and attitude.

The evaluation system, developed by Drs. Lynn Taussig, John Kattwinkel, William Friedewald and Paul di Sant'Agnese, establishes an excellent prognostic score as 91-100 points, a poor outlook of 60 points or below. To assure completeness, a clinical evaluation sheet is added to the score. This allows the reporting physician to indicate common complications which are not generally correlated with prognosis, and to review at a glance a patient's detailed past history.

The system supplies information not provided by existing methods, combines documentation of a patient's clinical status with a generally reliable numerical index for life expectancy, and also allows easy patient categorization for research purposes.

Respiratory Complications

The key to prolonged survival for most cystic fibrosis patients is control of respiratory complications. Chronic pulmonary disease is responsible for death in 90 percent of the cases. Vital respiratory function is the subject of a number of Institute-supported research projects. These include studies involving pulmonary ventilation, certain complicating, secondary respiratory disorders, cilia and ciliary movement, and bronchi and bronchial mucus in cystic fibrosis.

Seeking more effective medication for the lower respiratory tract, investigators are evaluating aerosol inhalation therapy. This type of treatment permits small particles of drugs essential for breaking up mucus to penetrate the lower lungs where the air passages are smaller but the surface area is greater.

In addition, research on antibiotics is continuing. A number of safe and effective drugs are currently in use; however, resistant strains of microorganisms, particularly *Pseudomonas* and *Staphylococcus*, pose problems in long-term antibiotic therapy. Investigations are underway to evaluate a vaccine against *Pseudomonas* infection as well as the long-term effectiveness of a semi-synthetic penicillin, carbenicillin. Institute investigators have also demonstrated the effectiveness of gentamicin against drug-resistant strains of these two organisms.

Identification of Carriers

A problem in prevention of cystic fibrosis is its method of hereditary transmission. Although effective screening tests have been developed for some other genetic disorders, such as Tay-Sachs disease and sickle cell anemia, a simple and reliable, precise method of detecting carriers of the cystic fibrosis trait has eluded investigators. In recent research, grantees Dr. Barbara Bowman of the University of Texas, Galveston, and Dr. Kurt Hirschhorn of the Mount Sinai Medical School, have developed new tests to identify carriers of cystic fibrosis; their reliability in *all* cases is as yet subject to future, long-term experience.

Dr. Bowman and her associates have isolated and identified a substance in the blood of both CF patients and carriers which inhibits ciliary action. Although the presence of this factor had been noted in 1967, investigators had been unable to isolate it from the blood serum until now.

Previous research had demonstrated that serum or serum fractions from cystic fibrosis patients and carriers inhibited ciliary action in rabbit trachea and in fresh water clams. Dr. Bowman has now tested the newly isolated material on the cilia in oyster gills with the same result. A similar test with blood serum using rabbit cilia, has been developed by Dr. Hirschhorn and associates.

The significance of the development of tests to identify carriers lies in their application for genetic counseling. When only one parent carries the cystic fibrosis trait, their children will not inherit the disease (although some will be carriers). If both parents are carriers, however, there is a one-in-four chance of cystic fibrosis occurring among their offspring. Since carriers exhibit no clinical symptoms of the disorder, a reliable and simple method of pinpointing them would be invaluable. Research is continuing to refine these and other tests which the investigators hope will be easily available.

Duodenal and Small Bowel Abnormalities in Cystic Fibrosis

The radiographic appearance of the duodenum and small bowel in cystic fibrosis has long been overlooked in the evaluation of CF patients. Recent research by Institute investigators emphasizes the importance of detecting abnormalities in these areas to avoid faulty diagnosis (particularly that of peptic ulcer) and unnecessary diagnostic procedures.

Duodenal barium studies of 33 cystic fibrosis patients revealed abnormalities in 84 percent of the subjects, a far greater frequency than previously reported. These consisted of markedly thickened folds, nodular indentations along the duodenal wall, poor definition of the mucosal fold pattern, and distortion and kinking of the duodenal contour. In contrast, irregularities in the jejunum and ileum were infrequent, and only rarely were findings compatible with previously reported "deficiency" or "malabsorption" patterns in cystic fibrosis.

The findings by Drs. Lynn Taussig, Ronald Saldino and Paul di Sant'Agnese indicate that the intestinal abnormalities associated with cystic fibrosis are found primarily in the duodenum. Malnutrition, quite common in untreated unrecognized cystic fibrosis patients years ago, may have accounted for some of the jejunal and ileal irregularities noted in the past.

The origin of the duodenal abnormalities is not clearly understood since no significant correlation with severity of disease, clinical symptomology or age could be discerned. The study has emphasized, however, a need to recognize radiographic abnormalities of the duodenum.

Increased IgA Production in Patients with Pancreatic Insufficiency

Recent reports suggest that cystic fibrosis may be associated with abnormalities of the immune system, in particular, the IgA immunoglobulin. Research by Institute investigators indicates that the production of IgA (the major immunoglobulin found in the plasma cells and in secretions of the gastrointestinal tract) is significantly greater than normal in patients with cystic fibrosis and hereditary pancreatitis. IgA production in cystic fibrosis patients also exceeds that of subjects with hereditary pancreatitis.

The data correlated with the degree of pancreatic insufficiency: cystic fibrosis patients had complete lack of pancreatic enzymes and the highest IgA values, while in hereditary pancreatitis, some exocrine pancreatic function remained and lower IgA values were noted. The study by Drs. Z. M. Falchuk and L. M. Taussig suggests that IgA concentration in the intestinal secretions may be increased by elevation in local production rather than by a retarded breakdown, possibly by pancreatic enzymes.

The mechanism by which increased intestinal IgA synthesis is related to pancreatic insufficiency is uncertain. It is possible, however, that the altered gastrointestinal environment may be due to the presence of certain proteins or other materials which are normally digested by pancreatic enzymes.

The investigators point out that cystic fibrosis does not of itself lead to a generalized stimulation of IgA production. Rather, the data support the hypothesis that increased IgA production in certain regions of the body is a secondary phenomenon in patients with this disorder.

Outlook

Although much has been accomplished toward alleviating the symptoms of cystic fibrosis, its basic defect and means of permanent control still elude investigators. Malnutrition due to pancreatic insufficiency, formerly a serious complication of the disease, can now be readily managed in most cases by administration of supplementary pancreatic enzymes of animal origin. Through improved antibiotic therapy the consequences of chronic pulmonary disease can now be forestalled in many patients. These measures, and others, have prolonged the life of the cystic fibrosis patient, and have also enhanced the quality of that still unduly short life.

Research is now focused on a wide range of problems. These include refinement of precise screening techniques to identify carriers of the cystic fibrosis trait; identification of the underlying metabolic defect in the disorder; and improvement of antibiotic therapy to retard the progression of chronic pulmonary disease, the most frequent fatal complication of cystic fibrosis. The findings of recent years are contributing to an increasing knowledge base from which the ultimate answer to the cystic fibrosis problem hopefully will come.

HEALTH SERVICES ADMINISTRATION
BUREAU OF COMMUNITY HEALTH SERVICES
Maternal and Child Health

While there is no cure for cystic fibrosis, intensive therapy, begun early, can control the disease, and make it possible for most patients to lead relatively normal, happy and productive lives.

Cystic fibrosis is an hereditary disease involving the exocrine (outward secreting) glands of the body, not only those which produce mucus, but also the sweat and salivary glands. It takes many forms, depending on the severity of the disease and the organs which are chiefly affected. Usually the most serious and the predominant complications are pulmonary. However, gastrointestinal symptoms may be the first to emerge in some patients. A reliable diagnostic test for cystic fibrosis is based on the abnormally high concentration of salt in the sweat of almost all patients.

The advent of antibiotics, advances in the understanding of pulmonary physiology, the development of the sweat test as an accurate diagnostic tool, and coincidentally the improved management of children with cystic fibrosis by teams of experts in special centers have resulted in marked reductions not only in mortality, but in the ill effects from the disease.

The treatments needed by children are both expensive and time consuming for families and patients. Since more than one child in a family may be afflicted and since the need for treatment is life-long, the cost (not including the emotional strain) to families of even moderate means may be beyond their own resources.

Because children are living longer and the need for treatment is life-long, in at least 2 States, Connecticut and Pennsylvania, the legislatures have appropriated funds for the care of persons over 21.

State chapters of the National Cystic Fibrosis Research Foundation whose headquarters are now in Atlanta, Georgia, have been active in promoting legislation favorable to patients with cystic fibrosis.

Because many children referred to special medical centers for cystic fibrosis are found not to have cystic fibrosis but rather some other form of chronic respiratory disease, a developing trend is for the centers to expand their research, teaching and service and change their name to "pediatric pulmonary" centers in order to reflect their expanded program.

On July 1, 1973 authority for administering 11 projects supporting Pediatric Pulmonary Centers was transferred from the Regional Medical Program Service to Maternal and Child Health/Bureau of Community Health Services. In addition to the ongoing administration of the projects MCH was charged with reviewing all of the Centers and formulating a report on the current status and future needs of such programs. Based on the review it is evident that there is a need for more trained health professionals, adequate clinical resources (such as appropriately equipped and staffed neonatal intensive care units), and organized systems for casefinding, transport of sick infants and followup services. Existing centers are addressing their efforts to meeting these needs.

Maternal and Child Health/Bureau of Community Health Services will continue to place special emphasis on providing the comprehensive array of health and related professions necessary for the full range of services related to the growth and development of all children, in addition to the care required by those with chronic pulmonary disease.

DIABETES

Recent diabetes research has emphasized studies of a fundamental nature designed to gain a better understanding of the underlying causes of the disease. The trend has continued during the past year, with the most important findings concerning an important advance in insulin assay technology, implication of the pancreatic hormone glucagon in the development of diabetes, further insight into the small blood vessel disease associated with diabetes, and encouraging research on pancreatic beta-cell transplants.

The knowledge that more than 4 million Americans suffer from diabetes, makes continued, intensive and effective research on this disorder an unceasing obligation on the part of scientists at the National Institute of Arthritis, Metabolism, and Digestive Diseases (NIAMDD), and investigators elsewhere supported financially by the NIAMDD.

Obligations for Programs in Diabetes

	1971	1972	1973	1974 Estimate	1975 Estimate
National Institutes of Health:					
National Institute of Arthritis, Metabolism, & Digestive Diseases...	$7,856,000	$8,182,000	$8,235,000	$10,937,000	$11,921,000

NATIONAL INSTITUTES OF HEALTH

National Institute of Arthritis, Metabolism, and Digestive Diseases

A complicated disease, for which there is no known cure, diabetes ranks seventh on the list of diseases causing death in the United States. Diabetes has been known for some time to be a hereditary disorder. As a result of the body's inability to metabolize carbohydrates normally (which, in turn, is related to impaired production or activity of the hormone insulin), the diabetic is unable to convert dietary carbohydrates properly into the stored form, glycogen, or to utilize them normally to produce the energy required for body functions. Thus, the carbohydrates, in the form of glucose, accumulate in the blood and, because of their high concentration, overflow into the urine. As the disease progresses, abnormal carbohydrate metabolism becomes associated with additional derangement in the metabolism of fats and proteins.

In its severe form, frequently called "juvenile type" diabetes because of its early onset in life, the untreated disease may rapidly progress to a grave metabolic state of imbalance, ketoacidosis, which may result in coma and death unless controlled by insulin administration and specific supportive therapy. Patients afflicted with its less severe form, the so-called "maturity-onset diabetes," may suffer from complications such as accelerated degeneration or "hardening" of the arteries, and thus may have decreased life expectancy. Although the disease can be fatal unless properly treated, in most cases the more obvious clinical symptoms can be controlled. Despite apparent control of these symptoms, however, progressive changes occur in both juvenile and maturity-onset diabetes that may lead to gradual deterioration of blood vessels, the kidneys, the nervous system and, particularly, the retina of the eye.

Diabetes, which may affect the blood vessels, eyes, nervous system, and kidneys, among other organ systems, is a prime example of a disease in which the research conducted by a number of the Institutes of the National Institutes of Health might be pertinent. Therefore the NIH is establishing mechanisms to assure a coordinated program of research by the several Institutes concerned with the various aspects of diabetes.

An Inter-Institute Committee on Diabetes is being planned with the Director, NIAMDD, as its chairman. Other Institutes represented on the committee include the NHLI, NEI, NINDS, NICHD and NIGMS.

Search for the Cause

Determining how insulin is produced and released by the pancreas and how it does its vital work in human tissues is essential to clarifying the cause of diabetes. In an important advance in assay technology in diabetes, Institute grantees Drs. Donald F. Steiner and Arthur F. Rubenstein of the University of Chicago have described the changing nature of insulin-secreting pancreatic beta-cells during insulin treatment of juvenile and adult-onset diabetes.

It is not uncommon to observe a transient remission, or "honeymoon" period, in patients with newly diagnosed juvenile diabetes. It has been assumed that this period of relatively easy disease control is due to a partial, temporary recovery of the insulin-secreting function in the beta cells of the pancreas. Assessment of such function by known methods in insulin-treated diabetics has been hampered, however, by the presence of antibodies to insulin in the patient's blood.

A method has been developed for measuring "C-peptide", a by-product of native insulin synthesis that is produced by beta cells in equal concentration with insulin. This unique method has permitted monitoring beta cell secretory products in the blood of insulin-dependent diabetic patients. These measurements have confirmed the long-held clinical impression that the remission phase in diabetes usually results from resumption of beta cell secretory activity.

The data obtained also confirm the existence of residual beta-cell secretory function in many insulin-requiring adult-onset diabetics, even after 5 to 10 years of insulin therapy. The ability to detect such subtle changes in beta-cell function by measuring C-peptide activity in the presence of native insulin and insulin antibodies could lead to a more rational therapeutic approach and ultimately improve the long-term outlook of this disease.

Possible Role of Glucagon

Three years ago an Institute-supported scientist at the University of Texas suggested that a pancreatic hormone other than insulin, glucagon, may play an important role in diabetes. Glucagon, heretofore, had been viewed as playing a relatively minor role.

Dr. Roger Unger's studies of the function of glucagon-secreting cells ("alpha-cells") in the pancreas of normal and diabetic subjects indicated that diabetes is characterized by a continuous state of relative or absolute glucagon excess. Because several actions of glucagon are antagonistic to those of insulin it was suggested that excess glucagon may exaggerate the metabolic consequences of insulin insufficiency, and may unfavorably influence diabetic control.

The same investigator now has shown that in nondiabetic subjects infection is accompanied by glucagon excess. Such an excess can worsen the diabetic state, which may explain the infection-induced deterioration frequently observed in diabetic patients. Such deterioration has traditionally been ascribed to insulin resistance.

Plasma glucagon was measured in nondiabetic patients hospitalized with bacterial infection, in healthy control subjects, and in dogs with experimentally induced pneumonia. The effects of induced glucagon excess also were observed in dogs with experimentally-induced diabetes controlled by insulin therapy.

Dr. Unger's studies clearly demonstrated that nondiabetic subjects with moderate and severe infection commonly exhibit striking glucagon excess. Infection, through the mechanism of glucagon excess, can bring about metabolic deterioration in dogs with experimental diabetes and, by implication, in diabetic patients despite plasma insulin levels normalized by insulin therapy. The mechanism by which infection causes increased glucagon secretion is as yet unknown.

In a related study Dr. Unger's observations in 26 consecutive patients hospitalized with diabetic ketoacidosis revealed that the 17 most severe cases had absolute glucagon excess, and the other nine had relative glucagon excess. Ketoacidosis is a grave metabolic state of imbalance, associated with poor disease control, that requires emergency therapy.

Glucagon levels in the blood were correlated with various measurements of the severity of ketoacidosis, such as blood glucose levels, breathing rates, and hours of insulin therapy required to correct the abnormality. Moreover, patients with absolute glucagon excess required significantly more insulin than the other patients. Glucagon levels declined after four hours of insulin treatment and were near normal upon discharge from the hospital.

Thus, there is an apparent relationship between glucagon excess and the severity of diabetic ketoacidosis. Although the nature of this relationship is as yet unclear, glucagon's natural antagonism to insulin may partly explain the remarkable degree of resistance to insulin which characterizes the initial treatment phase of severe diabetic ketoacidosis.

Small Blood Vessel Disease

The thickness of the basement membrane of certain muscular small blood vessels has been reported to be increased in adult-onset diabetes, and in one-half or more of those persons genetically predestined to develop diabetes ("prediabetics"). Few studies have been made, however, of basement membrane thickening (BMT) in patients with juvenile-onset diabetes.

New measurements in the latter type of patients show that BMT is rarely encountered during the first six years of the disease, but is almost always present thereafter. The data suggest that BMT is not inevitable in juvenile diabetes, but is related mainly to the duration of the disease.

Dr. T. S. Danowski of the University of Pittsburgh measured BMT in 15 patients with juvenile diabetes and in 50 control subjects without diabetes. These measurements were within normal limits in seven of the 15 patients, indicating that BMT is not an inevitable characteristic of juvenile diabetes.

BMT did correlate, however, with the duration of the disorder. Abnormal widths were seen in 7 patients with diabetes of 6 years duration or longer, while normal widths were seen in 7 of 8 patients with diabetes of less than 6 years duration. Also, since duration and age tend to be related, such thickening was more common in the older patients (over 20 years of age) with juvenile-onset diabetes.

Meanwhile, another NIAMDD grantee at Harvard Medical School, Dr. Robert G. Spiro, has compared basement membranes obtained from diabetic and nondiabetic kidneys. His studies revealed that diabetic kidneys contain more basement membrane-like material than nondiabetic kidneys, and that the chemical composition of these materials is quite different. It is suggested that the unique structure of basement membranes in diabetic kidneys may form the basis for the defective filtration process observed in long-term diabetes, which permits large quantities of protein to pass from the blood to the urine.

Pancreatic Beta-Cell Transplants

Hope for advances in the treatment of diabetic patients is indicated by recent work involving transplantation of islets of insulin-producing beta-cells isolated from the pancreas. Through selective culture of such cells or islets in laboratory tissue cultures, it may be possible to develop a preparation which will produce insulin once transplanted into the patient, and which may escape the rejection commonly observed with transplants of the whole pancreas.

Surgeons at the University of Minnesota have transplanted the entire pancreas into diabetic patients who were subsequently treated with immunosuppressive drugs. The transplanted organs were capable of secreting insulin for a number of weeks and the diabetes was improved temporarily. Although whole pancreatic transplants may not prove to be a very practical solution to the diabetic problem, because of the limited number of usable donors likely to be available, they further our understanding. To date, however, transplants of the entire pancreas have, on the whole, not survived more than one year.

We reported last year that Drs. Walter F. Ballinger and Paul M. Lacy of Washington University, St. Louis, had investigated the transplantation of insulin-producing pancreatic beta-cells from normal to diabetic rats. Transplantation of such cells into pockets in the thigh muscles or into the peritoneal cavity resulted in significant reduction of blood and urine sugar levels and restoration of weight gain in the host animals. Although the disease was not cured it was certainly modified and ameliorated. Microscopic studies subsequently revealed intact and functioning pancreatic cells in the transplanted rats, whose native pancreatic beta-cells had been destroyed experimentally, indicating that the animals were utilizing the transplanted cells. Here, too, however, inactivation of the transplanted beta-cells was observed eventually.

Dr. Arnold Lazarow, University of Minnesota, has now developed a new approach to the problem of transplanting insulin-producing cells with a greater potential for survival in the recipient patient. He and his associates have maintained pancreatic cultures under laboratory conditions for periods of up to ten days. They showed that beta-cells, grown in these cultures, are capable of synthesizing insulin and that they respond to high glucose levels by releasing extra insulin. They also showed in the diabetic rat that a single transplant of functioning beta-cells was effective in controlling all symptoms of diabetes for more than one year.

Dr. Lazarow's work has suggested that islets of cells derived from immature pancreases of newly-born animals can be transplanted to diabetic animals more successfully than those from older animals. He postulates that by starting with human embryonic pancreas it may be possible to reproduce islet cells in large numbers and to "direct" these cells, by appropriate environmental manipulation, to become insulin-producing cells. Quantities of cultured beta-cells might then be transplanted into human diabetic subjects. With an improved potential to control the host rejection, these transplanted cultures could function for months or even years, secreting insulin as the need arises.

Whenever such research approaches the point where effective long-term control of the symptoms of human diabetic subjects can be maintained by transplanted beta-cells, it will be important to determine whether such functioning transplants can prevent or delay the onset of the complications of diabetes, such as those affecting blood vessels, the eyes and the kidneys. If the complications of diabetes are prevented, beta-cell transplants might then provide a major advance in diabetes treatment.

OUTLOOK

Although the basic cause of diabetes is, as yet, unknown, there has been progress in clarifying some of its mechanisms. Institute scientists and grantees have broadened their fundamental studies of the pathology of diabetes, of the action of insulin, and of the many biochemical and physical changes which occur in body cells and fluids of diabetic patients. It now appears, for example, that diabetes may be a bihormonal disorder involving two pancreatic hormones, insulin and glucagon, and that the appearance of small blood vessel disease may presage the onset of diabetic complications.

NATIONAL INSTITUTES OF HEALTH

National Institute of Arthritis, Metabolism, and Digestive Diseases

DIGESTIVE DISEASES

Digestive diseases include such well-known disorders as peptic ulcer, regional ileitis, and ulcerative colitis, and encompass many other diseases of the intestinal tract and associated organs about which too little is known. These include cirrhosis of the liver, gallbladder disease, pancreatitis, and intestinal malabsorption.

Digestive diseases, which affect about 13 million Americans, are among the most common illnesses in this country, ranking second only to diseases of the heart and circulation in the number of resultant physician office visits or house calls. Cirrhosis of the liver, for example, is the fifth most common cause of death in male adults in America.

Obligations for Programs in Digestive Diseases

	1971	1972	1973	1974 estimate	1975 estimate
National Institutes of Health:					
National Institute of Arthritis, Metabolism, & Digestive Diseases...	$13,069,000	$16,404,000	$16,240,000	$19,835,000	$19,781,000

Peptic ulcer or its symptoms will strike about 10 percent of all adults in the United States at some time in their lives. Many victims of ulcerative colitis are afflicted for years with their disorder and eventually must undergo extensive surgery. Diseases of the stomach and intestines may afflict persons of any age, but most often affect those in the younger and middle-aged groups at the peak of their most vigorous and productive periods, often causing prolonged and expensive hospitalization and countless social and emotional problems.

The economic cost of digestive diseases is also significant. The annual economic loss in the United States due to peptic ulcer alone is estimated at just under $1 billion. The loss due to disability and lost income due to premature death, is calculated at $11 billion annually. Of all disease categories, digestive diseases rank third in causing economic loss, exceeded only by cardiovascular disease and accidents.

Money invested in digestive disease research has borne a rich harvest of fundamental as well as practical information, especially in relation to bile salt metabolism and gallstones, intestinal secretion and toxigenic and choleretic diarrheas, hepatitis-associated antigen and acute and chronic liver disease, the complex interaction of gastrointestinal hormones, and the motor and secretory disorders of the gastrointestinal tract - to mention only a few active areas of productive basic and clinical investigation.

There is considerable expectation that as this wave of interest and discovery in digestive diseases gains momentum we will be able to replace much of the empiric approach to therapy of digestive disease by rational therapy, based on an improved understanding of the pathophysiology of these disorders.

Because of the numbers of people affected, it seems likely that digestive diseases will continue to be cared for on many levels, as they are now. The research training needs for this category of disease are large. To ensure optimal care for patients with digestive diseases, new knowledge must be disseminated promptly and specialty advice must be timely and more widely available. Provision must be made for a continuing supply of motivated individuals for teaching and research so that understanding of digestive diseases continues to grow.

The National Institute of Arthritis, Metabolism, and Digestive Diseases (NIAMDD) bears the responsibility for the Federal Government's research in the field of digestive diseases. In 1973, NIAMDD contracted for a comprehensive task force of experts in gastroenterology to define the problems and needs in research. The evaluating body, consisting of eleven work groups, will recommend priorities as well as identify untapped areas for research.

Intramural research in digestive diseases in the laboratories and clinics of the Institute in Bethesda was given added emphasis by the reorganization of a Digestive Diseases Branch with four sections, including a new section on diseases of the liver.

Through numerous grants to scientists at research centers across the country, many ailments of the digestive tract are being studied. Research progress has been achieved through intensive and comprehensive laboratory experiments and clinical trials. This past year, these investigators have contributed many important research findings.

Dissolving Gallstones

Digestive diseases are as complex from the standpoint of the biomedical research investigator as they are from the point of view of the practicing physician. For example, little is known about how gallstones are formed, but gallstone disease ranks fifth among causes of hospitalization. About 15 million Americans are estimated to have gallstones; in many cases they cause no symptoms while in others they result in debilitating disease. Surgery is the standard form of treatment and some 375,000 gallbladder operations are performed each year at an average cost of $2000 each. Inasmuch as an estimated 6,000 patients die each year as a result of gallbladder surgery, a less drastic way of controlling the disease has long been sought.

About two years ago investigators supported by Institute grants reported that long-term oral administration of chenodeoxycholic acid (a natural bile acid) can result in dissolution of long-standing cholesterol gallstones.

In July, 1973 an initial contract was awarded to Cedars-Sinai Medical Center in Los Angeles to supervise and participate in a long-term collaborative clinical study of the feasibility, effectiveness and safety of dissolving gallstones with the aid of chenodeoxycholic acid. It is anticipated that the contract-supported study will run for five years and may ultimately cost several million dollars.

This is the first comprehensive study undertaken to determine the efficacy of a medication for gallstone dissolution and, through ancillary research, to find out how gallstones form and what causes their formation.

The stages of the study involve a planning period of one year, a treatment and ancillary study phase of three years, and a final phase devoted to an analysis of the data obtained. About 900 patients will be selected and treated at nine medical centers, some of these yet to be determined. Committees comprised of distinguished gastroenterologists and researchers throughout the United States have been formed to assist.

The chemotherapy approach, provided it is proven free of undesirable side effects, may offer an alternative to surgery for many patients with cholesterol gallstones and may save millions of dollars a year in hospital and related costs.

Bile Composition

Recent research has suggested that formation of cholesterol gallstones is due to secretion by the liver of bile relatively lower in bile salt content and supersaturated with cholesterol, which subsequently precipitates in the gallbladder. This important finding, which points to the liver rather than to the gallbladder as the origin of the disease, has channeled research efforts in a wholly new direction. As yet, however, the responsible liver defect has not been defined.

An Institute-supported grantee, Dr. Donald M. Small and associates of Boston University, showed that the abnormal hepatic bile secreted by patients with cholesterol gallstones reverts to normal following removal of the gallbladder, suggesting that this organ is essential for elaboration of abnormal bile. The explanation may be that the concentrated bile salts which enters the intestine upon gallbladder contraction, and which is largely conveyed to the liver via the enterohepatic circulation, "turns off" the normal rate of synthesis of bile salts in liver cells for a prolonged period.

Crohn's Disease Studies--

The Institute has in progress an in-depth study of Crohn's disease, or regional enteritis, a chronic inflammatory condition of the small intestine. This disorder causes severe pain, fever and weight loss, with prolonged periods of hospitalization, and frequently necessitates abdominal surgery involving removal of affected portions of the intestine. In about half the cases, the disease begins between the ages of 20 and 30.

Under Institute sponsorship, fourteen research centers across the country are now evaluating the therapeutic and prophylactic value of drug treatments in Crohn's disease. The National Cooperative Crohn's Disease Study is a controlled, randomized clinical evaluation of three drugs, prednisone, azulfidine, and azathioprine, to determine their respective efficacy. The study involves examining each drug's effectiveness in preventing intensification of the disease and determining the effect of each in preventing recurrence. Prompt treatment of this debilitating disease with an effective and suitable agent could transform an incapacitated, helpless and dependent person into a productive, self-supporting member of the community.

Surgery in Inflammatory Bowel Disease

Surgical resection of affected portions of the intestine to reverse growth retardation in children with inflammatory bowel disease does not seem justified, according to a study by Institute-supported grantees Drs. J. B. Kirsner and I. H. Roseberg at the University of Chicago.

Sixteen children, 10 with Crohn's disease and six with ulcerative colitis were studied; all had low height profiles. Ten underwent surgery, and six were treated medically. Yearly rate of growth was calculated for six years, three years before and three years after operation for those who underwent surgery, and from onset of disease for those who had medical treatment alone.

Only four of 10 of the surgery patients showed a greater than 100 percent yearly growth rate, and six of seven who are now adults are still shorter than their corresponding adult relatives. Five of the six patients treated medically are now adults, and two have attained normal height.

Folic Acid Deficiency in Inflammatory Bowel Disease

Folic acid deficiency complicating inflammatory bowel disease has been reported with variable frequency. Although several different mechanisms, such as dietary deficiency, increased tissue utilization, and malabsorption of folates (salts of folic acid) may be at work, there has been little information concerning this condition and its possible cause.

Research by Institute grantee Dr. I. H. Rosenberg and his associate, Dr. James L. Franklin of the University of Chicago, indicates that impaired absorption of folic acid is a factor in the origin of folate deficiency in inflammatory bowel disease, and that such malabsorption is aggravated by treatment with Azulfidine, one of the most commonly used drugs. Surveillance of folate status and correction of folic acid deficiency may be important in the treatment of patients, especially those treated with Azulfidine.

Controlling Diverticular Bleeding

Colonic diverticular disease is the most common form of massive, acute lower gastrointestinal bleeding. Such bleeding can usually be controlled with continued blood replacement. This is fortunate, inasmuch as those affected are usually elderly persons with coexisting diseases which make them poor surgical risks.

Institute grantee Dr. Stanley Baum of Massachusetts General Hospital, Boston, has shown that this gastrointestinal hemorrhage can be controlled by selective infusion of vasoconstricting drugs into the mesenteric artery, a procedure which has potential as an alternative to emergency surgery.

The research involved 15 patients with severe, unremitting diverticular bleeding who were considered medical therapy failures and, thus, candidates for surgery. Such therapy resulted in prompt control of bleeding in all cases. Seven of the 15 needed no further treatment; they have been observed for 6 to 30 months without recurrence of bleeding. Four patients eventually underwent surgery for bleeding that recurred subsequently after cessation of infusion treatment and 4 other patients eventually had elective surgery at different intervals afterwards.

Role of Modified Fatty Acids in Diarrhea

The precise cause of the diarrhea observed in patients with steatorrhea (abnormal fecal fat loss) is not known. Increased quantities of hydroxy fatty acids have been found in the stools of such patients, however, and it has been suggested that they may be the mediators. Institute grantee Dr. Henry J. Binder and associate Dr. Peter Bright-Asare of Yale University, is attempting to determine if hydroxy fatty acids can alter colonic salt and water absorption.

Results indicate that ricinoleic acid, the primary fatty acid in castor oil, causes considerable net secretion of water, sodium, and chloride into the rat colon. Oleic acid, a non-hydroxylated fatty acid, did not induce net secretion but did inhibit net absorption from the colon. These findings support the hypothesis that hydroxylated fatty acids may have a role.

Peptic Ulcer

Some of the most exciting research in peptic ulcer revolves around gastrin, the hormone which stimulates secretion of gastric juices. The synthesis of gastrin accomplished by Institute grantees in previous years has provided an important tool for studying peptic ulcer, in which an excess of acid digestive juices is secreted. Since then, another group of grantees has shown in rats that experimental induction of immune antibodies against gastrin can inhibit the potent gastric acid stimulatory action of gastrin. This suggests possible novel approaches to counteracting excessive gastric acid secretion in human disease states such as peptic ulcer.

For example, Institute supported grantees Dr. J. E. McGuigan of the University of Florida and his associate, Dr. W. L. Trudeau have shown that patients with duodenal ulcers exhibit greater increases in serum gastrin levels than do normal persons in response to feeding. This finding emphasizes the potential importance of this hormone in duodenal ulcer disease, the most common form of peptic ulcers.

In earlier studies, the investigators were unable to detect increased serum gastrin concentrations in duodenal ulcer patients during the fasting state, although their gastric acid secretory rates were elevated. Comparison of serum gastrin levels in duodenal ulcer patients and in normal persons after a protein-rich meal, however, has revealed levels significantly greater in the duodenal ulcer patients.

The Kidney and Gastrin

Gastrin is known to be removed from the circulation quite rapidly whether administered intravenously or normally secreted by the stomach. A recent study showed that 40 percent of synthetic gastrin administered to dogs is extracted and degraded by the kidney; it has not been determined, however, if natural gastrin suffers a similar fate.

By inducing secretion of endogenous gastrin in dogs, Institute grantee Dr. Warren D. Davidson of Harbor General Hospital, Torrance, California and associates have now found that 30 percent of gastrin entering the renal artery is extracted by the kidney, while less than 2 percent of the extracted hormone is subsequently found in the urine. The evidence indicates that the kidney plays an important role in the extraction and degradation of gastrin, as it does for insulin and a number of other polypeptide hormones.

Promising Peptic Ulcer Treatment

Histamine, well known to allergists as part of the immune defense mechanism, can dilate capillaries, stimulate smooth muscle, precipitate hives and induce other inflammatory and allergic reactions. It also stimulates secretion of gastric acid in the stomach. Conventional antihistamine drugs are incapable of counteracting this gastric acid secretion, but recently a British team has been successful in developing a new drug, Metiamide, which can block the effect of histamine on the heart, the uterus and the stomach, and can thus mitigate histamine's enhancement of gastric acid secretion.

The first human trials with Metiamide are being conducted both in Britain and in the United States. Preliminary results obtained in the United States by Drs. Morton Grossman and Jon Isenberg of the Wadsworth VA Hospital, Los Angeles, indicate the efficacy of single oral doses of the drug in sharply reducing gastric acid secretion, without any apparent undesirable side effects, in 15 patients who were known hypersecreters of gastric acid. A similar effectiveness was shown in a patient with the Zollinger-Ellison syndrome, a condition characterized by the pathologic secretion of extremely large quantities of gastric acid. These results are preliminary and must be viewed with caution at this early stage, but the hope exists that a new class of drugs has been developed to produce sufficient inhibition of gastric acid secretion without noticeable undesirable side effects.

Digestive Enzymes and Lipids

It is generally believed that dietary triglycerides (the common edible fats and oils) are not appreciably affected by enzymes until they reach the duodenum. Research by Drs. Margit Hamosh and Robert O. Scow of the Institute showed that the serous glands of the rat tongue secrete a potent enzyme that converts dietary triglyceride to partial glycerides (mostly diglycerides) and free fatty acids in the stomach. It is assumed that this reaction is the first step in the digestion of dietary lipid. Preliminary studies indicate that a similar salivary enzyme is present in man.

LIVER DISEASE

The liver performs a multitude of complex biochemical tasks without which life cannot exist. The largest single organ in the human body, the liver functions as a "chemical factory," as a clearing station for purification and detoxification of blood, as a storage house for certain nutrients (particularly carbohydrates, certain minerals, and vitamins), as a site of production of blood proteins, as a secretory gland which aids both digestion and the removal of wastes, as well as for a myriad of other metabolic functions. Not surprisingly, an organ of such complexity is subject to a great many injuries and diseases.

Hope for Victims of Biliary Atresia

Biliary atresia, a rare illness which affects one out of every 25,000 newborns, may become rarer still due to a new approach developed by a research team headed by Institute grantee Dr. Norman B. Javitt, Cornell University Medical College.

Biliary atresia is the term used to describe the condition when infants are born without bile ducts. These children usually die after several months to several years because of resultant cirrhosis. Cholestatic syndromes, diseases such as biliary atresia, characterized by the absence of bile flow from the liver to the intestinal tract, represent a difficult diagnostic and therapeutic problem for patients of any age.

The researchers found that many children who seem to have biliary atresia have instead another condition - a metabolic flaw that reduces the liver's capacity to make bile. Because of this abnormality the bile ducts remain underdeveloped; in fact they can be so small that they may not be recognized at surgery. Often, these children can be treated by medications that correct the metabolic insufficiency and permit the ducts to develop.

The Cornell doctors also developed a new method of analyzing minute amounts of bile salts in blood. This replaces an older method which required taking undesirably large amounts of blood from the newborn. The new method permits precise determination of each of the bile salts by gas-liquid chromatography, and aids in the differential diagnosis between true biliary atresia (non-formation of bile ducts) and impaired formation of bile, a process which may require several repeated determinations of bile salts in the blood.

Alcohol Metabolism in the Liver

Institute scientists at the NIAMDD research unit at the Phoenix, Arizona, Indian Medical Center, and collaborating scientists at the Indiana University School of Medicine, have been investigating in American Indians (Pima) and white subjects,differences in the activity of the liver enzyme alcohol dehydrogenase, which plays an essential role in the normal degradation and metabolism of imbibed alcohol. Their work indicates that a significant difference exists between alcohol dehydrogenase activity in their Indian and white patients, the former being quite low. Differences in rapid chemical degradation of imbibed alcohol by this enzyme would determine the ease with which an individual can handle more than ordinary amounts of alcohol without a buildup of alcohol to intoxicating levels.

Bypass Corrects Atresia

In another important advance, a team of American surgeons including grantee Dr. R. P. Altman at the Children's Hospital, Washington, D. C. successfully applied a surgical procedure developed in Japan for the correction of biliary atresia. The surgery involves making a bile duct from a segment of the intestine. The result of this procedure is to bridge effectively the blocked bile duct. The present operation offers a promising advance to save significant numbers of these patients.

Outlook

The National Institute of Arthritis, Metabolism, and Digestive Diseases is committed to a broad and diverse research attack on disorders of the gastrointestinal system. The new impetus given gastroenterological research is due not only to active Institute support but to the productive roles played by the scientists it supports through research grants and contracts. Their new ideas, techniques and research findings will result in a more complete understanding and improved treatment for the millions of individuals afflicted and disabled with digestive disorders.

NATIONAL INSTITUTES OF HEALTH

National Institute of Arthritis, Metabolism, and Digestive Diseases

NUTRITION

The National Institute of Arthritis, Metabolism, and Digestive Diseases (NIAMDD) bears the principal responsibility for medically oriented nutrition research supported by the Federal Government. In addition to direct research activities in its laboratories and clinics in Bethesda, the Institute supports nutrition research projects through grants to research centers throughout the United States and abroad. These activities cover the full spectrum of nutrition research, from fundamental metabolic and physiologic studies, to programs designed to determine how best to alleviate malnutrition and nutritional deficiency diseases.

Obligations for Programs in Nutrition

	1971	1972	1973	1974 estimate	1975 estimate
National Institutes of Health:					
National Institute of Arthritis, Metabolism, & Digestive Diseases...	$6,571,000	$7,887,000	$7,896,000	$8,580,000	$9,344,000

State of the Art

The role of nutrition in medicine and health has changed over the past few decades. In previous years, nutritional diseases such as scurvy, beriberi and rickets posed serious health problems in clinical medicine. Fortunately, through research on corrective treatments and public education on proper diet, these disorders are no longer a menace to the American population.

Attention is now turned to the problems of obesity and malnutrition, both of which are increasing throughout the U. S. At the present time, the health of millions of Americans is impaired by various dietary excesses or deficiencies. Poor nutrition, more importantly, accounts for mental difficulties, physical impairments and increased susceptibility to other diseases.

In light of these facts, nutrition research has become increasingly involved with development of low-cost, high quality foods which may be instrumental in stemming the tide of undernutrition both in this country and abroad. On the opposite end of the spectrum is research into the causes, management and prevention of obesity, which experts now believe has reached epidemic proportions in the United States. Research has produced a variety of approaches to help obese patients achieve weight loss, including, for extreme cases, total starvation and surgical ileo-jejunal bypass operations as well as weight reduction by behavior modification. In the future, NIAMDD intends to create multidisciplinary centers for clinical and basic research on obesity.

Investigators are now examining the role of trace elements such as zinc, iron, chromium, silicon, fluorine and others, to determine their essentiality to health. Also under study are numerous vitamins, their roles in proper growth and development, and the consequences and correction of deficiences.

The scope of nutrition research has broadened and deepened over the years to include new emphasis on the definition and diagnosis of malnutrition. Evaluation of nutritional status is no longer dependent on ill-defined symptoms or on the subjective judgment of the examining physician.

The study of nutrition continues, however, with the enthusiasm that marked its first advances - the discovery of vitamins and nutrition-deficiency diseases fifty years ago. Investigations this past year have added to our knowledge base of human nutrition in health and disease, and also have indicated extensive need for research in chronic nutritional disorders.

Scope of Research

The research grants program of the NIAMDD is divided into two classifications - physiology of normal nutrition, and nutritional disorders. Projects in the physiologic processes of normal nutrition involve study of body composition, digestion and absorption of nutrients in the gastrointestinal tract; appetite regulation and food intake; the biochemistry and physiological role of nutrients and their fate in the body; quantitative requirements for proteins and amino acids, carbohydrates, fats and fatty acids, minerals, trace elements, vitamins, and fluids and electrolytes; interrelationships between different nutrients and between nutrients and hormones, and nutrients and enzymes; and the relationship of the intestinal flora to nutrition.

Research in abnormal nutrition involves discovery and definition of deficiency states, nutrient toxicity, obesity, malabsorption of specific nutrients, and investigation of the relationship of diet to specific disease entities, such as celiac disease. Other research relates to nutrition in specific diseases or stress states, such as in diabetes, bone and joint disease, liver disease, gastrointestinal disease, infectious diseases, disorders of immunity, anemia, endocrine disorders, gallbladder disease, inborn errors of metabolism, skin disorders, kidney disease and kidney stones, and stress (including surgery, trauma, wound healing and environmental extremes).

Research Accomplishments

Zinc: A Trace Element Essential in Vitamin A Metabolism

A grantee and a scientist of the NIAMDD have demonstrated in animal studies that normal mobilization of vitamin A from the liver and maintenance of normal plasma levels of the vitamin depend upon the presence of zinc.

In research by Dr. J. Cecil Smith, Jr. of George Washington University and Ernest G. McDaniel of NIAMDD's Laboratory of Nutrition and Endocrinology, rats sustained on a zinc-deficient diet evidenced markedly lower plasma vitamin A levels than the normal control group. This finding suggests that the vitamin was not being mobilized from the liver.

In subsequent experiments, rats fed only vitamin A demonstrated significantly higher liver concentrations of the vitamin and markedly lower plasma vitamin A levels than rats fed the vitamin plus zinc. The investigators also found that when the vitamin was permitted to accumulate in the liver, zinc therapy resulted in its mobilization from the liver into plasma, indicating that zinc is required for maintaining normal plasma levels of vitamin A.

These data suggest that patients with depressed plasma levels of the vitamin who are unresponsive to vitamin A therapy may respond to additional zinc supplementation.

Renal Production of the Biologically Active Form of Vitamin D

The site of production of the metabolically active form of vitamin D (cholecalciferol) has long been the object of intense investigation. Recent research by NIAMDD grantees showed conclusively that the conversion of cholecalciferol to the metabolically active form, 1,25-dihydroxycholecalciferol, takes place in the kidney.

Vitamin D is essential for intestinal absorption of calcium and its mobilization from bone. In their research, the investigators found that the stimulation of these processes is five to ten times greater with the more active metabolite than with an equivalent amount of cholecalciferol.

Ronald J. Midgett, Anthony Norman and associates at the University of California, Riverside, Wadsworth Veterans Administration Hospital, Los Angeles, and the UCLA School of Medicine demonstrated that the conversion process to the active form of vitamin D requires two metabolic steps. The circulating intermediate, 25-hydroxycholecalciferol, is first produced by the liver. The biologically active metabolite 1,25-dihydroxycholecalciferol is then synthesized in the kidney from the intermediate.

The investigators have presented evidence indicating that the synthesis of 1,25-dihydroxycholecalciferol is universal among mammals, and that the kidney thus serves as an endocrine gland involved in the regulation of calcium metabolism.

In clinical application, the fact that the human kidney is capable of producing the "hormone" suggests that vitamin D-resistant osteomalacia observed in chronically uremic patients may result from the kidney's inability to perform this function. The researchers have reported successful use of the active metabolite in stimulating serum calcium levels and intestinal calcium absorption in uremic patients.

Analogs of 1,25-Dihydroxyvitamin D_3

NIAMDD-supported investigators at the University of Wisconsin have demonstrated that analogs of the active vitamin D metabolite, 1,25-dihydroxyvitamin D_3, stimulate intestinal calcium transport and bone calcium mobilization in anephric rats (whose kidneys have been removed).

The metabolite itself manifests these properties, but the length and expense of its chemical synthesis prompted an examination of analogs that might be less expensive and less difficult to prepare.

Dr. Hector F. DeLuca and associates produced two derivatives of the vitamin D metabolite which demonstrate the ability to stimulate intestinal calcium transport and bone calcium mobilization in anephric rats. The analogs 5,6-trans-vitamin D3 and isotachysterol$_3$ evidenced their potential use in the treatment of hypocalcemia (subnormal calcium level in the blood), impaired intestinal calcium transport, osteodystrophy (degeneration of normal bone) due to kidney dysfunction, and secondary hyperparathyroidism (abnormally increased activity of the parathyroid glands causing loss of calcium from the bones). Of the two, isotachysterol$_3$ can be converted and purified more simply and economically, and therefore holds promise for eventual use in cases of renal osteodystrophy.

Role of Amniotic Fluid in Fetal Development

Recent research by Institute grantees Drs. Donald Orlic and Robert Lev indicates that amniotic fluid which surrounds and protects the fetus may also conduct nutrients, medications or other compounds of potential benefit to the growing fetus.

In studies by the New York Medical College investigators, radioactive iron was injected into the amniotic sacs of near-term rat fetuses. The iron in the amniotic fluid was swallowed by the fetuses and within hours, was detected in the intestine, liver and spleen. These findings demonstrate that substances added to amniotic fluid may be readily transported to the fetal circulation for use in developing organs.

The implications for human fetal development are great. In a near-term human fetus, approximately half of the total amniotic fluid is swallowed and cycled in a 24-hour period. Thus it may become possible to provide nutrients to the fetus via the amniotic route in cases of maternal deficiency, or, conceivably, to inject antigens to trigger a prenatal immune response.

This research was also supported by the National Institute of Child Health and Human Development.

Iron Fortification of Food

Recent research by NIAMDD grantee Dr. Richard B. Walker demonstrated that iron fortification of foods is likely to be effective only in individuals who take animal protein as part of their diet, inasmuch as fortification iron added to vegetable foods shows very limited absorption.

Two forms of iron, "heme" and "nonheme", are absorbed differently in the body. The intestinal absorption of heme iron (derived from ingested animal muscle and blood) is apparently not influenced by dietary composition. The availability of nonheme iron (such as iron salts added to flour as an enrichment measure), however, is greatly dependent on dietary consumption. In studies conducted by the University of Washington, Dr. Walker provided conclusive evidence of the enhancing effect of meat on the absorption of nonheme iron, based on multiple absorption studies performed on 228 persons from test meals containing foods of either animal (veal muscle) or vegetable (maize) origin which were tagged biosynthetically with iron supplements.

The findings suggest that the lack of animal protein in the diets of some underdeveloped nations may play an important role in the iron deficiency noted in large segments of these populations, even when the vegetable-based local diet appears to contain sufficient iron on the basis of laboratory analysis.

Special Nutrition Research Studies

Specific research projects, carried out abroad among populations with nutritional deficiency diseases, are designed to find solutions to complex malnutrition problems. These projects are largely funded through the U. S. - Japan Cooperative Medical Sciences Program and through Public Law 480 "Counterpart Funds," U.S.-owned local currencies in developing countries derived from the sale of surplus agricultural commodities. Only half of the earth's population maintains an adequate diet, indicating a critical need for research to find ways and means to transform marginal nutrition and overt nutritional deficiency to adequacy.

Traditionally, the Institute has conducted nutrition research in developing countries because of the availability of large population groups afflicted with specific nutritional deficiencies which can be readily studied. The results from such research are two-fold: It may stimulate emergence of self-sufficiency from mere subsistence in Southeast Asian countries, for example, and may also add knowledge of normal nutrition and nutritional deficiencies that will benefit the U. S. population.

The startling realization that malnutrition does, in fact, exist within our own population lends an element of expediency to nutrition research. But by providing scientific know how for effective utilization of economical, indigenous protein sources, these programs also discourage dependency of developing countries on the United States for expensive protein-rich foods and enable them to make inroads against endemic protein malnutrition.

Southeastern Asia

The mission of the nutrition segment of NIH's U.S.-Japan Cooperative Medical Sciences Program is to support research aimed at practical solutions to nutrition-related problems in Korea, India, Pakistan and other nations in the Pacific basin. The substantial grant and contract program already has brought significant findings to improve the protein level of rice, the principal food of 60 percent of mankind. Ordinary commercial rice lacks sufficient protein for normal growth and development of children maintained on a predominantly rice diet, and does not protect the adult population from serious protein under-nutrition. Research identified approximately 100 rice varieties which contain from 6 to 10 percent more protein than the present conventional level of 7 1/2 percent. Breeding and growing experiments are continuing to identify which of these high-protein varieties are most agriculturally and commercially suitable to the Southeast Asian setting.

Protein Malnutrition Studies in India

NIAMDD sponsors a vital research and development project in India, funded by Public Law-480 U. S. surplus commodity funds, to study protein malnutrition, intermediary metabolism and selected metabolic disturbances in kwashiorkor (protein malnutrition) patients.

Studies at the Christian Medical College in Vellore including fortification of wheat with lysine, the first, most limiting amino acid in the nutritionally incomplete wheat protein. During a six month experimental period, children on a lysine-supplemented wheat diet grew significantly in height compared to the children in a control group not given the supplement. This investigation represents the first conclusive clinical finding that lysine fortification of wheat protein, when it is the only source of dietary protein, can significantly improve the growth of preschool children. It also demonstrated the potential benefit of an inexpensive method of improving protein nutrition that is not dependent on educating a population toward better nutrition (a slow procedure at best), or on changing local dietary habits.

Investigators at Vellore noted that after 6 to 8 months of life, the growth rate of breastfed Indian babies failed to keep pace with that of children in more developed countries. Research established that a weaning food supplement based on native cereals and containing inexpensive peanut protein fortified with methionine (an amino acid essential for optimal growth) can serve as an adequate source of protein for growing infants. Infants fed the vegetable weaning food maintained comparable growth rates with a milk food control group.

An NIAMDD-supported project at the Central Food Technological Research Institute in Mysore involved laboratory development of food supplements based on inexpensive, indigenous protein sources to prevent kwashiorkor prevalent among preschool children in India. This research led to development of Miltone, a protein-rich product combining buffalo or cow milk with peanut protein isolate which has the potential of doubling the available milk supply. Other studies demonstrated that many native cereal foods fortified with peanut flour acquired a significantly higher biological value and could serve as a nutritionally adequate, inexpensive source of food for growing children.

FOOD COMPOSITION TABLES

The third in a series of regional food composition tables was recently published by the Institute in cooperation with the Nutrition Program of the Center for Disease Control (CDC) of the Public Health Service and the Nutrition Division of the United Nations Food and Agriculture Organization.

The two-volume set, entitled "Food Composition Table for Use in East Asia" and "A Selected Bibliography on East Asian Foods and Nutrition Classified According to Subject Matter and Areas," is an essential tool for nutritional assessment of dietary consumption of the population.

Supported by U. S.-Japan Cooperative Medical Science Program funds, the current project follows the earlier publication of Food Composition Tables for Use in Latin America (1961) and Africa (1968). Distributed world-wide, the regional food tables have been employed by national and international institutions.

Overseas Nutrition Research

Scientific findings emanating from nutrition research abroad hold practical application in this country. Of importance are the contributions concerning intermediary metabolism during protein deprivation and vitamin deficiency which could not have been conducted adequately in the U.S. due to a lack of sufficient patient material in any locality. These efforts also contribute specifically to the technological knowledge of the American food industry.

Traces of the mold aflatoxin, for example, have been found in U.S.-made peanut butter. There is considerable importation of peanuts (which may be contaminated with aflatoxin) to the United States from abroad, and little is known concerning aflatoxin contamination in many U.S. feeds.

Technologic achievements in aflatoxin destruction through special processing methods developed in the Institute's Mysore project are of importance in the United States.

The aim of such projects is to assist a developing country in achieving a state of self-sufficiency. Rather than creating a dependency on the United States for gifts of expensive protein-rich foods, these programs provide the scientific know-how for effective utilization of inexpensive proteins which the host country can produce itself. Such measures will enable the country to cope more successfully with the problem of protein malnutrition, and to correct the disproportion between population increase and agricultural self-sufficiency.

Research accomplishments resulting from overseas studies not only enrich the fund of scientific knowledge in the United States, but also enhance the image of American science through dissemination in American scientific literature. These projects demonstrate effective use of U.S.-owned counterpart funds (PL-480 funds) in biomedical studies, illustrating the value of this support mechanism which demands no current expenditures of U.S. funds.

Outlook

Improved methods of evaluating nutritional adequacy have contributed to a new emphasis on the definition and diagnosis of malnutrition. Evaluation of nutritional status is no longer dependent on ill-defined symptoms or on the subjective judgment of the examining physician.

The study of nutrition continues with the enthusiasm that provided its first advances, the discovery of vitamins and nutrition-deficiency diseases fifty years ago. Although the investigations this past year have proven productive in adding to our knowledge base of human nutrition in health and disease, they have also indicated new areas for much-needed research in chronic nutritional disorders. The Institute is anticipating more significant advances in these research efforts in the coming years.

ARTHRITIS, RHEUMATIC DISEASES, AND ORTHOPEDIC SURGERY

Dr. **Lamont-Havers.** Rheumatoid arthritis is the most crippling form of arthritis. We would like to discover how the disease progresses and what exactly is the mechanism by which it destroys normal tissue. Our efforts have been concentrated toward finding a possible infectious agent, perhaps a virus, underlying the disease, and toward elucidating the specific nature of the malfunction in the immune system of the body which seems to lead to rheumatoid disease.

We are not convinced, however, that immunological studies alone are certain to produce the ultimate definition of this disease and we are consequently pushing forward our support on as many fronts as appear logical and promising. In the meantime, we shall continue our research on therapy in our struggle to find ways to control arthritis and relieve its victims.

There is no specific therapy for the treatment of osteoarthritis, the degenerative form of arthritis which appears with advancing age. The most severe cases may require reconstruction surgery to correct damaged joints, or total replacement of nonfunctioning joints with artificial prostheses, as is being done with increasing success in the case of hip joints and knees. Our scientists will continue to assemble data from extensive trials of total hip and knee replacement, employing both new and conventional materials. Ceramic materials will be compared with stainless steel, and various types of bone cements will be evaluated. These studies eventually should point to optimal procedures in both hip and knee replacement and aid in other arthritis related surgery.

DIABETES AND OTHER METABOLIC DISEASES

Despite the fact that diabetes has been controlled in millions of people for many years, it remains a serious and complicated disorder of metabolism, ranking seventh on the list of disease causing death in the United States. We shall continue our drive to gain a better understanding of the mechanism of action of insulin, of the intricate details of carbohydrate and fat metabolism in the disease, and of the precise nature of the blood vessel abnormalities which underlie its major complications. We are also concerned with exploring ways to suppress development of complications of diabetes which include enhanced atherosclerosis and consequent coronary heart disease and circulatory failure in the extremities, as well as nerve damage, kidney failure and blindness.

Our research will cover studies on the role of the hormone glucagon, since excess glucagon release appears to have a detrimental influence on diabetes control, and the highly exciting, though preliminary, work on pancreatic islet beta-cell transplantation in animals; despite the great theoretical potential of this work, however, a great deal of progress must be made in transplantation immunology before human transplantation of pancreatic islets can be considered as a therapeutic tool. We expect to expand our support of Diabetes-Endocrinology Research Centers. These centers are expected to provide core resources and services at an institution where a broad and substantial volume of excellent diabetes research already exists and will be used to strengthen and to permit further development of these efforts.

In the meantime, we are pursuing our research on a number of other metabolic diseases, including cystic fibrosis, a grave, familial disease of young children, Hurler's and Hunter's syndromes, which are similar hereditary disorders of mucopolysaccharide metabolism characterized by skeletal deformities, mental retardation and early death, and Fabry's disease, a herditary disorder of glycolipid metabolism.

ENDOCRINE DISORDERS

Hormones, the secretions of the endocrine glands, control or regulate some of the most basic metabolic processes of the body and profoundly affect the functioning of its organ systems, both in health and disease. Because of the importance of knowing the precise mechanism of hormonal action on cells and tissues, we support many basic studies on hormone action as well as more clinically oriented investigations of the diseases caused by hormonal imbalance. Our clinical studies include investigations of such abnormalities as osteoporosis, hypopituitary dwarfism, acromegaly, thyroid disorders, adrenal dysfunctions, among others.

In recent years, our grant-supported scientists isolated a chemical agent from the brain, called somatostatin, which inhibits growth hormone release by the pituitary gland. Later, they were able to demonstrate that synthetic somatostatin effectively inhibits secretion of growth hormone in experimental animals. In new research, these same investigators have now shown that synthetic somatostatin inhibits growth hormone secretion in both normal persons and in patients with the hyperpituitary disease, acromegaly. If a long-acting preparation could be developed, this agent might have value as a means of decreasing the excessive growth hormone secretion associated with acromegaly and other disorders such as gigantism. This is an example of the promising developments which make the field of endocrinology such an important aspect of our research program.

HEMATOLOGY

The study of blood diseases is an important part of the research program of the Institute. This reflects serious concern for the many Americans afflicted with killing and disabling blood disorders, including blood clotting disorders such as hemophilia, and the familial anemias, such as Cooley's anemia.

In cooperation with other research efforts at NIH, NIAMDD is developing expanded programs of research, diagnosis, prevention, and treatment of Cooley's anemia. This disorder is the most common of the thalassemias, a group of genetically determined blood disorders, the main biochemical defect of which is inability of the body to produce red blood cells with sufficient biologically active hemoglobin. One effort involves the serious problem of excess iron storage in the vital organs of patients with Cooley's anemia who have received therapeutic blood transfusions over a long period. The search for nontoxic agents to remove the dangerous and inadvertent deposits of iron, which cannot be eliminated by normal processes, is a major research goal.

DIGESTIVE DISEASES

Digestive diseases such as peptic ulcer, ulcerative colitis and numerous other disorders of the pancreas, gallbladder and liver afflict millions of Americans each year and are actually among the most common chronic and disabling diseases that we know. They are also complex disorders, both from the viewpoint of the practicing physician and from that of the biomedical researcher.

For instance, little had been discovered about the cause of gallstone disease until recent research suggested that formation of cholesterol gallstones is due to secretion by the liver of bile deficient in bile salts and supersaturated with cholesterol which subsequently precipitates in the gallbladder. This important finding, which points to the liver rather than to the gallbladder as the origin of the disease, has channeled research efforts in a wholly new direction. As yet, however, the responsible liver defect has not been defined. In the meantime, we will continue promising studies of treating cholesterol gallstones medically rather than surgically by using the natural bile acid, chenodeoxycholic acid, to dissolve the stones or prevent their formation in patients known to be stone formers.

In peptic ulcer research, our grant-supported investigators have shown in preliminary clinical trials that metiamide, a histamine analogue developed in Great Britain, may be of value in reducing excess gastric acid secretion. Although these results are still viewed with cautious optimism, we hope that metiamide represents a truly physiological approach to peptic ulcer control and one that may be the forerunner of new and effective anti-ulcer agents.

In still other preliminary research, our grantees have produced for the first time what seems to be alcoholic hepatitis in baboons by giving them alcohol in combination with a nutritionally adequate diet. Since alcoholic hepatitis often precedes alcoholic cirrhosis in man, it will be important to see whether the baboons eventually develop cirrhosis. These and other studies promise to reveal whether alcoholic hepatitis is the link between fatty liver (a reversible condition) and cirrhosis (which represents endstage damage), as many scientists believe it is. We have also produced evidence suggesting that alcohol consumed by chronic drinkers might have an injurious effect upon cells of the small intestine strikingly similar to the damage to liver cells which often occurs in alcoholic people.

NUTRITIONAL DISEASES

Nutrition research, one of the oldest programs of the Institute, continues to be an important area of accomplishment and requiring continuing attention. Our program activities encompass the spectrum of nutrition research from basic metabolic and physiologic studies to those directed toward relief of malnutrition and nutritional deficiency diseases. In the latter area, we are particularly interested in iron deficiency anemia, which is especially prevalent among female teenagers and women of childbearing age. Presently there is interest in increasing the iron level in enriched flour in order to improve iron balance or to prevent iron deficiency anemia. Recent research indicates that absorption of such iron from enriched flour is likely to be effective only in people who eat animal protein concomitantly—an interesting aspect which, I believe, has not been considered heretofore.

In the meantime, research to facilitate prevention and control of obesity will continue to be supported by the Institute. Overweight and obesity to a degree that interferes with optimal health and longevity affects more than 20 percent of adults in the United States.

UROLOGIC AND KIDNEY DISEASES

Nearly 8 million Americans suffer from diseases of the urinary tract, and each year some 58,000 people in the United States die of irreversible kidney failure. The Institute supports numerous studies in the search for new knowledge with which to prevent, control, or cure the various diseases of the kidney. During the past year, which has brought passage of the new amendments to the social security law, a major effort has been made to advance developments in kidney transplantation and artificial kidney dialysis to help fulfill the promise of the new medicare provision that effective transplantation or dialysis treatment will be provided to all endstage kidney patients eligible under the social security laws.

The success of the medicare treatment program in treating all of these patients optimally and decreasing their number in years to come depends greatly upon the research and development projects supported by the Institute.

These efforts include clinical trials of new dialyzers, development of special adsorbents for uremic toxins, and development of a new shunt for implantation in dialysis patients, one which is compact, offers faster blood flow, less clotting and fewer complications than indwelling blood vessel connections now in standard use.

In the field of kidney disease research, investigators have shown that an androgen hormone, fluoxymesterone, when given orally improves the anemia associated with chronic renal failure. In other studies, grantees have found evidence of an association between virus infection and transplant rejection in kidney patients. These investigators believe that the high incidence of viral infection among transplant patients may result from suppression of the patient's protective immune mechanisms due to drugs administered in an effort to avoid rejection of the grafted organ. Other scientists are conducting further studies in hope of finding ways to reduce the incidence of graft rejections not only in cases of kidney transplants, but among liver and pancreas transplant patients as well.

I should also mention that we are planning a broad front of research related to kidneys and the urinary tract in an effort to diminish the incidence of urologic disorders and kidney diseases and to curtail significantly the number of patients who require drastic end-stage kidney disease treatment.

DERMATOLOGIC DISORDERS

In the field of skin disease, we have available a number of drugs developed for chemotherapy of cancer and we shall continue to screen and develop them for possible use in the topical treatment of severe psoriasis. We will also encourage studies to examine the clinical implications of the recently reported low cyclic AMP levels in the skin lesions of psoriasis patients.

Recently our scientists have indicated that the drug azaribine may be of value in treating severe psoriasis and studies have shown promising results in 75 percent of patients treated and at least some benefit in 90 percent of those receiving treatment with the drug. Other dematologic disorders are also being studied with support from the Institute, including such diseases as stopic dematitis, pemphigus, and discoid lupus erythematosus.

In conclusion, Mr. Chairman, I am submitting an overall request for 1975 of $152,961,000. I am looking forward to another year in which we shall continue the Institute's sound and productive pursuits in health research.

Thank you. I shall be happy to answer any questions the committee may have.

ALLOCATION OF FUNDS

Mr. Flood. I would like to mention last year's report. We said this on page 34 of last year's report of this committee:

"During the past year, one of the scientists at the Institute's Bethesda laboratories, Dr. Christian B. Anfinsen, won the Nobel Prize in chemistry for his pioneering research that has illuminated some of the most important principles regarding the chemical structure and catalytic activity of an enzyme. Concurrently, one of the Institute's grant-supported investigators, Dr. Gerald M. Edelman of Rockefeller University, was awarded the Nobel Prize in physiology and medicine for research in immunology." Doctor, your budget, as I am sure you must know, is the subject of intense interest, if I may understate, on the part of quite a number of organizations and groups and subgroups all interested in a specific disease. They knock at my door and say "Don't raise any taxes, we want the budget balanced, but"—when I hear that but—"take care of us." That is the problem we have.

These people, quite properly so—you understand they are not fakers, but good, sincere, dedicated, in there dying for Rutgers for that one thing.

These groups are interested in arthritis, digestive diseases, sickle cell anemia, and Cooley's anemia, and psoriasis, and cystic fibrosis, and others I haven't mentioned.

Each one has its own vigorous advocates, and each year we have these organizations come in as public witnesses after you are through for the Government.

They tell us their disease is not receiving adequate attention. So my question is, what kind of decisionmaking process goes on at your Institute to determine how much money to allocate to each one of these diseases? How in the world do you decide that? I don't know if you want this in the record, but who decides it?

Dr. Lamont-Havers. This obviously is a continuing process. It certainly isn't done at any one time. Certainly such decisions are made, and there are a number of elements which go into that decisionmaking.

First of all, of course, we have to look at the resources which we believe will be available to us because obviously we have to fit everything into that one budget.

We then have to consider what our noncompeting commitments are, the commitments which were set up in previous years.

Then I think what we really do is to look at what areas should be receiving attention either because increased public concern is expressed in the Congress, or the administration, primarily through the Congress, rarely through the administration, or from the evaluation studies which we have done, that the time is ripe to give emphasis.

In the last 2 or 3 years obviously we have recognized the congressional concern for digestive diseases which has certainly been expressed, lately also for diabetes. And therefore we have tended to give a disproportionately greater distribution of funds in these areas during the past few years. There is a series of considerations which go into our determinations.

Mr. Flood. I thought so but I wanted you to say so.

Dr. Lamont-Havers. That is right.

Mr. Flood. In the 1975 budget you allocate $22,397,000 to arthritis, bone, and skin disease; and $46,858,000 to diabetes, endocrinology, and metabolism; $26,650,000 to digestive diseases and nutrition; $17,335,000 to the kidney diseases; and $10.5 million for hematology. Can you tell us how you arrived at those specific numbers?

Dr. Lamont-Havers. These obviously are mixtures of the amounts which are expended both in our extramural programs in grants, that amount in contracts, and that amount in our intramural program. So, therefore, the first thing we determined was, as I say, what were the commitments which had already been set up in these areas for the future. This was determined.

We then looked at the relatively "free" funds which would be available for us for distribution. We realized obviously that each area should receive a basic amount of support. We obviously could not differentially decrease the support in any one area because there is excellent research and excellent studies to be supported in every area.

Mr. Flood. The specifics is what I want.

Dr. Lamont-Havers. I think the specificity of the numbers by and large are arrived at as to what the commitments were, that usually is in odd numbers. Therefore, if you then divide up the amount of money you have left, otherwise not committed, those tend to be in rounded dollars. It is commitments which tend to make things odd.

Mr. Flood. Suppose the digestive people come to us and say, they are spending 22½ percent of the budget on digestive diseases, spending 38 percent on diabetes or whatever it might be. What do we tell them?

Dr. Lamont-Havers. What we tell them——

Mr. Flood. What do we tell them?

Dr. Lamont-Havers. We tell them that within the resources which we have available to us it is our best judgment, considering all of the factors which I have described, that this is the amount of money which we feel should be spent in these areas, and the fact is that resources are limited and everybody wants more of the same resources and so somebody has to make a decision as to exactly what will happen, and that is us.

Mr. Flood. And you give them a couple of aspirins and they go out?

Dr. Lamont-Havers. They usually don't leave quite that quickly.

1975 BUDGET

Mr. Flood. Your budget for 1975 is less than the amount appropriated for 1972, 1973, and 1974. Would it be fair to say that as a result of inflation—you have heard about that—we are actually supporting less research on arthritis, metabolism and digestive diseases than we were 10 years ago, 5 years ago?

Dr. Lamont-Havers. Probably the actual research effort was at its peak in about 1967 or 1968. Since then the ravages of inflation have tended to move in and in fact by and large cut down, up until the 1974 appropriation. At that time we began to turn around somewhat.

Mr. Flood. The answer is "yes," it is right?

Dr. Lamont Havers. Sort of yes.

Mr. Flood. All right. That is a new one.

What appropriation will be required in view of all of this to support the same level of effort which you supported in appropriations of $113,344,000 for fiscal year 1965? You said 1967 and 1968. I am going back to 1965. What would be the appropriations needed for that?

Dr. Lamont-Havers. I am talking off the top of my head. We can supply those specifically for the record, but at that time we were funding approximately 60 to 65 percent of approved research grant applications. We are now funding about 45 percent. So therefore there is a differential there of some 15 percent.

[The information follows:]

Based on U.S. Bureau of Labor Statistics cost of living index, the programs of this Institute which were supported at a level of $112,886,000 in 1965 would require about $175,126,000 to maintain that level in 1974.

Mr. Miller. Mr. Chairman, may I make one point? If you look on page 179 in the justifications——

Mr. Flood. I did.

TRAINING GRANT PROGRAMS

Mr. Miller. You can see that the issue really is an issue that you have explored several times. It has to do with training grants. I think this Institute shows a significant amount of new work every place in the budget but a very sharp decrease in training grants. So the issue revolves around training grants.

Mr. Flood. I want to ask this: All through these hearings we have been trying to elicit from somebody, elevator operators, anybody, some persuasive arguments for the policy of phasing out training programs and substituting the postgraduate fellowships. So far, frankly, we haven't been able to detect any hair raising enthusiasm for this policy from anybody at NIH. Do you want to take a shot at it?

Dr. Lamont-Havers. My explanation as to why the training grants are phased out?

Mr. Flood. I want a persuasive argument as to phasing out the training grants program and replacing it with the doctoral fellowship program.

Dr. Lamont-Havers. I will give you an argument; I don't know if it is persuasive or not.

I am sure you have heard before as to the reasons behind this. I would believe that the new fellowship program is a realization that in order to support biomedical research programs in this country we have to have training and obviously we have to support training, and for reasons which undoubtedly are very good reasons the decision was made.

Mr. FLOOD. It is obvious this policy did not originate at NIH. Can you tell us whose idea it is?

Dr. LAMONT-HAVERS. I was not in on that policy——

Mr. FLOOD. I don't mean a name. Where did it come from?

Dr. LAMONT-HAVERS. I was not in on the policymaking decision that took place at that time.

Mr. FLOOD. That takes care of that.

Last year we added $2,761,000 to your budget to maintain the training grant programs at the 1972 level. In spite of all of that we are told the arthritis program is down to 41 training this year from 84 in 1972. What happened to all of that money? I have asked this question three times of others. You have been sitting here and you certainly ought to have an answer by now.

Dr. LAMONT-HAVERS. The answer to that question is that under the so-called old training program, which is still being phased out, the number of the trainees in the arthritis program was 60 in 1973, 50 in 1974, and 4 in 1975. That is clear.

However, in addition to that we do have postdoctoral fellowships and research career development awards, and also this year we will begin to support fellows under the new training program. Therefore, in fiscal year 1974, the present fiscal year, we will be supporting some 81 individuals in arthritis but that will come down to about 45 next year.

Mr. FLOOD. Suppose we were to appropriate more money for these training grant programs. Could they be revived? What institute would you call on to breathe some life into this? Can they be revived or by the time we pass the appropriations bill and it is signed by the President will rigor mortis set in?

Dr. LAMONT-HAVERS. We certainly effectively revived many of them this year with the additional funds. I am always amazed at the flexibility of the biomedical community, and I am sure they would adapt to any additional stimulus.

NUMBER OF TRAINEES SUPPORTED

Mr. FLOOD. Put in the record a table showing the number of trainees and the number of fellows supported through the appropriations for fiscal years 1972 right through and including 1975, and break them down by their own scientific field.

Dr. LAMONT-HAVERS. Very good.

[The information follows:]

NATIONAL INSTITUTE OF ARTHRITIS, METABOLISM, AND DIGESTIVE DISEASES—NUMBER OF FELLOWS AND TRAINEES BY SCIENTIFIC FIELD

	1972	1973	1974	1975
Arthritis:				
Fellows	13	12	22	32
Trainees	60	50	4	2
Dermatology:				
Fellows	10	14	21	31
Trainees	74	65	43	11
Diabetes:				
Fellows	19	14	16	14
Trainees	31	25	20	5
Endocrinology:				
Fellows	30	32	42	48
Trainees	120	113	75	20
Digestive diseases:				
Fellows	11	13	28	37
Trainees	104	96	74	19
Hematology:				
Fellows	16	11	29	47
Trainees	102	100	58	15
Metabolism:				
Fellows	59	52	44	31
Trainees	69	53	47	12
Nutrition:				
Fellows	6	9	13	9
Trainees	35	27	25	7
Orthopedics:				
Fellows	10	8	17	19
Traniees	32	24	18	5
Physical biology and related areas:				
Fellows	5	3	3	0
Trainees	32	21	16	4
Kidney diseases:				
Fellows	36	26	36	47
Trainees	106	100	66	16
Total:				
Fellows	215	194	271	315
Trainees	765	674	446	116

ANNUAL COST OF DIALYSIS

Mr. Flood. What is the current average annual cost per patient for dialysis?

Dr. Lamont-Havers. If you don't mind, I will ask Dr. Burton, the expert on that.

Dr. Burton. I think, Mr. Chairman, I better give it to you in ranges. The cost varies considerably depending on the place where the patient is being treated. Home dialysis is the least expensive. There is also dialysis in so-called limited care centers, a dialysis center into which you walk in and out and get your treatment there. Finally, there is dialysis in the hospital.

Let's start with the most expensive one, which is the traditional one, in the hospital itself. A patient is usually treated about three a week on the average, for about 6 or 8 hours per espisode of treatment. In the hospital this sort of treatment has a charge of anywhere from $250 to $350 per treatment. The reason for that is that the hospital charges bed cost for the full day and the hospital overhead is such that the price is high. If we multiplied that by 150 we get the yearly cost for that patient, $37,500, and that is a bona fide figure.

Mr. Flood. I have heard something like that; $35,000 is what they say publicly.

Dr. Burton. It can even be higher because if that particular hospital is a profitmaking institution, it is likely to be a little higher. At university hospitals that is a usual figure.

Let's proceed to the next one, representing the majority group of patients. I would say that half the patients in the country are being dialyzed in walkin dialysis centers, so-called limited care centers. Such a center doesn't have to be under the roof of the hospital; it may be free standing several blocks away or even in a downtown office building. In Bethesda there is one in an office building. In such a center the patient is being charged anywhere from $120 to $220 per treatment.

Mr. FLOOD. Can paramedics handle this?

Dr. BURTON. There the treatment is primarily by paramedics with one physician in attendance. The physician is needed to satisfy State health requirements and to handle emergencies.

The yearly treatment there ranges from $18,000 to $26,000.

Then there is the patient who looks to the physician as being capable, a patient who has a suitable home environment and a spouse that lives in with him, because you have to have two people for home dialysis. This patient will be trained to do dialysis by himself and the spouse in the home. That will be the least expensive of all, and cost of treatment ranges from $3,500 to $4,000, the absolute cheapest, to about $7,000 a year.

DIALYSIS TRAINING

Mr. FLOOD. Where is the wife or husband as the case may be or the oldest daughter or whatever going to go to get that kind of training? How long will it take, about?

Dr. BURTON. The training usually takes up to 6 weeks. It involves both the close relative or the live-in relative and the patient, and is very expensive and the cost can vary anywhere from $6,000 to $12,000 for their training.

Mr. FLOOD. Where are they going to get the training?

Dr. BURTON. They get the training either in the hospital, if that happens to be the knowledgeable center in that region, or at a special walkin limited care center where there is a physician in attendance who together with the dialysis nurse will give him that training.

Mr. FLOOD. I am sure you are worrying about this. We all are. What progress are we making toward getting those staggering costs down across the board for the treatment in any one of those centers plus the training for the home person, and what are we doing in finding any more effective methods of hemodialysis itself physically, hardware or anything?

Dr. BURTON. At the National Institutes of Health we have a specialized research and development contract program which addresses itself to that problem. One, improve the hardware, two, the methodology, and three, research in uremia which cuts across the entire area and makes the treatment more effective and cuts down the medical complications of that treatment. As you know, the treatment itself is not ideal. At best it is lifesaving and life-maintaining.

Mr. FLOOD. Are you just as much concerned about this as you are about the treatment itself?

Dr. BURTON. Yes, sir, we are.

Mr. FLOOD. Mr. Conte.

Mr. CONTE. Why is the cost of training some family member or other person so high?

Dr. BURTON. That comes as a shock even to us, but it comes about because it lasts anywhere from 4 to 8 weeks. These two people are usually in the hospital, one of them in the bed, and so you have daily hospital bed charges of about $100. They live in. Also—they require considerable, expensive staff time.

Mr. Flood. Are you working with the Social Security Administration on this?

Dr. Burton. Yes, quite closely. The Social Security Administration and the Bureau of Quality Assurance of the Public Health Service and we are usually in close communication on the matter of the Government-funded kidney disease treatment which started July 1, 1973. One of the strongest aims is to make the treatment (1) more effective, (2) less expensive.

To give you a good example, as I said, the treatment takes place about three times a week, lasting usually between 6 and 8 hours. If we could get a machine and methods of treatment which would cut that in half so the patient could be treated for only 3 or 4 hours per episode, the overall costs per year would come down considerably because trained labor is one of the biggest components of the cost.

DIALYSIS EQUIPMENT

Mr. Flood. The hardware itself too. I happen to be on Defense Appropriations, among other things. I remember years ago when we first came out with these computers in the Pentagon they were as big as this room. You had to climb up ladders and they had red and wellow lights. You would think it was a gambling joint. It was as big as a room. Now they are about the size of that table doing exactly the same thing.

Miniaturization is the thing they are talking about. The only trouble with that when they have the long haired hardware in Defense or anyplace they sell it to school boards or the hospitals, and it is delivered on Saturday. Then on Monday along comes a salesman and says that is obsolete, here is a new one for another $100 million.

What about miniaturization. Is it conceivable for this kind of hardware?

Dr. Burton. In fact we have had already made one quantum jump along that line. When our Institute started with this program the existing hardware was clumsy, large, hard to work with. Since that time we have, through Government funds, developed the first small, compact artificial kidney which is in production for the last 2 years and represents a real quantum jump.

Mr. Flood. Transportable?

Dr. Burton. That particular dialyzer that has been developed and is in operation is the size of a quart of milk. Not to give you the wrong impression, that is not the entire machine. In addition to that, again through research contracts from our program, a portable artificial kidney machine was developed in the sense of a portable television set which means it may strain you to move it from room to room, but you can move it.

Dr. Stone. Mr. Chairman, I would like to say that Dr. Burton and his colleagues, as recently as last week, convened a group to try to estimate what the ideal level of dialysis would be if there are no changes in technology. That is, how do we prevent an overutilization which might be stimulated by the funds in the system, or underutilization by those controlling the spending of funds. They are trying to establish standards by which one can measure an ideal level of dialysis. That would give us another administrative way of controlling the expenditures of funds. It would be automatically taken up by the PSRO mechanism as a standard against which care will be measured.

COOLEY'S ANEMIA

Mr. **Flood**. Doctor, we could keep you here all day talking about progress in prevention and treatment of these various diseases. I won't do that. A great deal is covered in the budget justifications and the special reports you supplied the committee with. But I do have a series of questions here on Cooley's anemia which Congressman Giaimo has asked me to address to you. I would like you to consider them carefully and provide the answers for the record.

[The information follows:]

Mr. **Flood**. The National Cooley's Anemia Control Act requires that the Secretary, HEW, carry out a program to develop information and educational materials relating to Cooley's anemia and to disseminate such information and materials to persons providing health care and to the public generally. What educational materials have been developed and disseminated and could you provide us with copies?

Dr. **Lamont-Havers**. After passage of the Cooley's Anemia Act, the Health Services Administration established contact with the National Cooley's Anemia Foundation to seek advice in the planning of programs relevant to Cooley's anemia.

Shortly after this beginning, the Agency underwent a period of reorganization resulting in the Health Services Administration assuming the responsibility for Cooley's anemia. It is only now that the Bureau of Community Health Services and Health Services Administration is in a position to concentrate on forward planning in this area.

Mr. **Flood**. The National Cooley's Anemia Control Act also requires the Secretary to establish a program within the Public Health Service to provide for voluntary Cooley's anemia screening, counseling, and treatment. This requirement, however, is dependent upon an effective and inexpensive screening test. Because the development of an effective and inexpensive test is so vital to the fulfillment of the provisions of the act, and because its development was specifically mentioned in the act, I would like answers to the following questions.

How many grants and contracts have been awarded for the development of an effective and inexpensive screening test?

What has been done to stimulate grant applications and contract proposals in this area?

The appropriation authority of the act expires at the end of fiscal year 1975. What is Health, Education, and Welfare's timetable for the (1) development of an effective and inexpensive test, (2) establishment of programs for Cooley's anemia screening, treatment, and counseling, and (3) establishment of a program for the development and dissemination of educational materials relating to Cooley's anemia?

Dr. **Lamont-Havers**. The subject of the availability of an inexpensive screening test and the need for screening and counseling programs were discussed in great depth at the research workshop in Cooley's anemia which was held in New York City in April 1973 by the National Institutes of Health Inter-Institute Coordinating Committee on Cooley's anemia. At that time the problems arising from the screening and counseling programs of sickle cell anemia were emerging and, because of the similarity between sickle cell anemia and Cooley's anemia, it seemed wise that the lessons learned from the sickle cell screening programs should be applied to that of Cooley's anemia. Consequently, the workshop participants recommended, and the National Institutes of Health Inter-Institute Coordinating Committee on Cooley's anemia agreed, to postpone development of a mass screening technique until the sociological effects and advisability of a mass screening program was determined by means of carefully controlled, small scale pilot screening and counseling programs. Presently available screening techniques are adequate for such small scale programs. While such pilot programs in screening and counseling were not the primary responsibility of the National Institutes of Health, when it became evident that such programs were not being initiated by other agencies, the National Institutes of Health, and specifically the National Heart and Lung Institute, began to develop the plans for implementing such a program. Since it was too late to consider this in the National Heart and Lung Institute research plans for fiscal year 1974, the program has been submitted in the National Heart and Lung Institute forward program for fiscal year 1975, for consideration within the priorities for that Institute's total research program.

Meetings are planned within the next month to 6 weeks to delineate programs for the establishment of a program for the development and dissemination of educational materials relating to Cooley's anemia. These meetings will occur to restore the working interface with the programs of the National Institutes of Health.

Mr. Flood. The first annual report on the administration of the National Cooley's Anemia Control Act lists 39 research projects applicable to Cooley's anemia. Budgetary constraints have caused the National Institute of Arthritis, Metabolism, and Digestive Diseases, which supports most of these 39 projects, and other institutes of the National Institutes of Health to make across-the-board reductions in the funding of research projects.

How many of these 39 projects were started after passage of the National Cooley's Anemia Control Act?

Dr. Lamont-Havers. Four of these projects were started after passage of the act: two by this Institute, and one each by the National Heart and Lung Institute and the National Institute of General Medical Sciences.

Mr. Flood. How many of these 39 projects had their budgets reduced because of the across-the-board reductions?

Dr. Lamont-Havers. This Institute supported 21 of the 39 projects. The general pattern in fiscal year 1974 was to reduce all awards on the average of 12 percent below the recommended level. Restoration is presently being made, where feasible, to projects reduced in fiscal years 1973 and 1974. The eighteen grants supported by the other institutes were not administratively reduced.

Mr. Flood. Instead of reducing the funding of these projects, why wasn't the authority of the act used to request money to fund the projects for their full amounts?

Dr. Lamont-Havers. In fiscal year 1973 Health, Education, and Welfare was operating under a continuing resolution since appropriation bills had been vetoed. It was considered that the amount of funds which were allocated for the support of biomedical research were appropriated to its priority within the Federal budget. Under these circumstances the administration did not consider it realistic to seek additional funds through other authorities.

Mr. Flood. During the last 18 months, several grants on Cooley's anemia research were approved on the basis of scientific merit but not funded. (See Comptroller General's report dated February 26, 1974, page 4, paragraph 3).

Does the National Institutes of Health consider Cooley's anemia research a high enough priority item to request funds under the authority of the act that was designed specifically for that purpose?

Dr. Lamont-Havers. The administration feels and so testified that the authorities under section 301, title III of the Public Health Service Act are entirely adequate to support biomedical research including that for Cooley's anemia and that no additional authority is needed.

RESTORED 1973 FUNDS

Mr. Flood. Also we want a breakdown of the $24,530,000 appropriated in 1973, but obligated in 1974, with an explanation of how these funds were being used. And a breakdown of those grants and contracts funded in 1974 for more than 1 year with the dollar amount involved there. Then, of course, also in your case—it is on page 179—revise that table in the justifications to include the 1973 funds obligated in 1974 and to reflect that multiple-year funding of grants and contracts. Also give us the comparable figures for 1972 and 1973.

Dr. Lamont-Havers. Yes.

[The information follows:]

NATIONAL INSTITUTE OF ARTHRITIS, METABOLISM, AND DIGESTIVE DISEASES

Obligations by Budget Mechanism
Showing "True" Program Levels
in 1974 - 1975
(Amounts in thousands)

	1972 Comparable Actual		1973 Comparable Actual		1974		1975	
Budget Mechanism	No.	Amount	No.	Amount	No.	Amount	No.	Amount
Grants								
Regular								
Non-competing	1,237	$62,638	1,322	$68,331	1,135	$67,838	1,264	$75,327
Competing	340	18,352	201	14,708	476	22,136	277	18,250
New	277	10,819	124	6,499	222	16,416	212	15,166
Supplemental	(187)	1,784	(133)	1,774	(34)	400	(42)	500
Subtotal	1,854	93,593	1,647	91,312	1,833	106,790	1,753	109,243
Special								
Multi-disciplinary centers	---	---	---	---	---	---	---	4,000
Research career programs	---	3,659	---	3,722	---	3,665	---	2,440
Scientific evaluation	---	256	---	256	---	256	---	300
Subtotal	---	3,915	---	3,978	---	3,921	---	6,740
Total Grants	1,854	97,508	1,647	95,290	1,833	110,711	1,753	115,983
Fellowships								
Non-competing	63	569	72	611	56	500	155	2,023
Competing	15	156	5	52	13	118	---	---
New	137	1,356	46	515	273	3,004	160	2,000
Supplemental	---	---	---	---	---	---	---	---
Subtotal	215	2,081	123	1,178	342	3,622	315	4,023
Training Grants								
Non-competing	210	12,523	190	9,441	175	12,696	39	1,506
Competing	36	2,014	37	2,017	---	---	---	---
New	10	397	5	118	46	2,322	---	---
Supplemental	(21)	138	(18)	174	---	---	---	---
Subtotal	256	15,072	232	11,750	221	15,018	39	1,506
Laboratory & Clinical Research		18,316		19,159		21,245		22,064
Research & Development Contracts		6,265		6,646		7,649		8,475
Biometry, Epidemiology & Field Studies		1,071		1,053		1,239		1,249
Research Management & Program Services		4,646		4,830		5,756		5,908
TOTAL		144,959		139,906		165,240		159,208

NATIONAL INSTITUTE OF ARTHRITIS, METABOLISM, AND DIGESTIVE DISEASES

Obligations by Budget Activity
Showing "True" Program Levels
in 1974 - 1975
(Amounts in thousands)

Budget Program	1973		1974		1975	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Arthritis, Bone and Skin Diseases................		$21,862		$25,825		$23,591
Diabetes, Endocrinology and Metabolism...........		43,261		50,513		49,313
Digestive Diseases and Nutrition.................		21,990		29,033		27,918
Kidney Diseases..................................		17,443		19,426		18,110
Hematology.......................................		10,308		12,203		11,055
Intramural Laboratory and Clinical Research.......	476	20,212	451	22,484	451	23,313
Research Management and Program Services..........	111	4,830	106	5,756	106	5,908
Total..	587	139,906	557	165,240	557	159,208

NATIONAL INSTITUTE OF ARTHRITIS, METABOLISM, AND DIGESTIVE DISEASES

Distribution of 1973 Impounded Funds
(Amounts in thousands)

Budget Mechanism	No. of Awards	Amount	Remarks
Research Grants:			
	42	$2,587	Arthritis, Bone and Skin Diseases
	87	5,331	Diabetes, Endocrinology and Metabolism
	44	2,692	Digestive Diseases and Nutrition
	26	1,619	Kidney Diseases
	19	1,185	Hematology
Total, grants	218	13,414	
Fellowships:			
	9	80	Arthritis, Bone and Skin Diseases
	32	293	Diabetes, Endocrinology and Metabolism
	19	173	Digestive Diseases and Nutrition
	4	34	Kidney Diseases
	7	60	Hematology
Total, fellowships	71	640	
Training:			
	12	840	Arthritis, Bone and Skin Diseases
	13	972	Diabetes, Endocrinology and Metabolism
	9	627	Digestive Diseases and Nutrition
	6	427	Kidney Diseases
	6	456	Hematology
Total, training	46	3,322	
Research and Development Contracts:			
		175	Diabetes, Endocrinology and Metabolism
		800	Digestive Diseases and Nutrition
Total, contracts		975	
TOTAL		18,351	

NATIONAL INSTITUTE OF ARTHRITIS, METABOLISM, AND DIGESTIVE DISEASES

Multi-year Funding from
1974 Appropriation
(Amounts in thousands)

Budget Mechanism	No. of Awards	Total Amount	Amount Affecting 1975 Funding	Remarks
Research Grants:				
	21	$2,424	$1,212	Arthritis, Bone and Skin Diseases
	44	4,910	2,455	Diabetes, Endocrinology and Metabolism
	22	2,536	1,268	Digestive Diseases and Nutrition
	14	1,550	775	Kidney Diseases
	10	1,074	537	Hematology
Total, grants	111	12,494	6,247	

SPECIAL DISEASE LEGISLATION

Mr. Flood. I am sure you are familiar with the disease of the month syndrome. You talk about your syndromes and your disease of the month things. We have one of our own. Congress seems to be falling into the habit of enacting special laws to direct attention to specific diseases. Many people feel this is the only way to keep the disease they are interested in from losing out in this competition for scarce appropriations and scarce resources and so on.

Since you are a catch-all in your shop, do you have any suggestions for the prevention, treatment and cure of this syndrome?

Dr. Lamont-Havers. No; because I feel that it is the right of anybody in America to come before Congress and state what they feel is their right or what they would like to see Congress do. I can't suggest anything which would prevent that happening.

Mr. Flood. Doesn't a budget which increases funds for cancer and heart disease at the expense of research in other diseases aggravate the situation by encouraging the idea that the only way to get money is to pass a special law preferably to have your special disease taken out of the jurisdiction of NIH altogether?

Dr. Lamont-Havers. I don't think that would have ever occurred to anybody until through a series of events a precedent had been set, in which case everybody else gets the idea they are just as special as the disease that was chosen. So therefore they want the same recognition for their particular area as was given elsewhere. I think it is the precedent setting which is the problem.

Mr. Flood. Mr. Conte.

Mr. Conte. Thank you, Mr. Chairman.

I would like to congratulate Dr. Lamont-Havers. I really enjoyed the way you handled yourself. Anybody that can parry that well with the chairman is pretty good in my book.

LEADING CAUSES OF DEATH

Would you give me some estimates of the total number of people suffering from diseases and the disorders covered by your Institute and compare that with the other major NIH Institutes?

Dr. Lamont-Havers. Yes, sir. We will provide that for the record.

Mr. Conte. All right.

[The information follows:]

10 leading disease-related causes of death (compounded from various sources)

Ranks and disease category	*Annual incidence*
1 Heart disease	741, 000
2 Cancer	333, 000
3 Stroke	208, 000
4 Kidney failure	58, 000
5 Influenza and pneumonia	56, 000
6 Certain diseases of early infancy	48, 000
7 Diabetes	38, 000
8 Cirrhosis of the liver	32, 000
9 Other bronchopulmonic diseases	31, 000
10 Other diseases of the circulatory system	30, 000

Note.—Accidents at about 115,000 per year are the true 4th leading cause of death.

EXTENT AND ECONOMIC IMPACT OF DISEASES

Mr. CONTE. Do you have any figures on the annual death rate and dollar costs of disabilities from the diseases covered by your Institute?

Dr. LAMONT-HAVERS. Yes, we do and here again if you don't mind, I will make them available for the record rather than try to do it now. The reason I say that is we have such a laundry list of diseases it would be quite a document.

[The information follows:]

EXTENT AND IMPACT OF MAJOR DISEASES OF NIAMDD

	Estimated number of patients in United States	Estimated loss to economy (GNP) (millions)
Arthritis	17,000,000	$4,000
Cystic fibrosis	30,000	
Orthopedics	26,000,000	
Cooley's anemia	50,000	100
Diabetes	[1] 2,800,000 [2] 1,600,000	2,000
Digestive diseases	13,000,000	8,100
Kidney disease	8,000,000	
Psoriasis	[3] 4–8,000,000	1,000

[1] Known.

[2] Not diagnosed.

[3] Estimated 800,000 have psoriatic arthropathy (a crippling form of arthritis).

HUNTINGTON'S DISEASE

Mr. CONTE. Do you do any research on Huntington's disease?

Dr. LAMONT-HAVERS. I think you will find that in the next Institute

ARTIFICIAL PANCREAS

Mr. CONTE. I understand that some of the important work on the development of the artificial pancreas was done under one of your training programs. Is that true?

Dr. LAMONT-HAVERS. Yes. We did have a training program in Boston and indeed some of our trainees did work on that particular project at the Joslin Clinic.

Mr. CONTE. Can you give us something for the record on what they developed?

Dr. LAMONT-HAVERS. Yes, sir.

[The information follows:]

DEVELOPMENTAL RESEARCH ON AN ARTIFICIAL PANCREAS

The majority of diabetes patients suffer from maturity-onset diabetes, a relatively mild and stable form of diabetes with onset in the adult or advanced years. Fortunately most of the patients with maturity onset diabetes do not require insulin shots for control of their disease. On the other hand, patients afflicted with the so-called juvenile-onset diabetes, a very serious disease, must have daily injection of insulin in order to keep their disease under control. Not only are these injections unpleasant, but even more important, this type of treatment tends to provide to the body more insulin than it needs right at the time of injection and less than it needs as the hours go by. The ideal treatment would be one where the artificial supply (by injection) of insulin to the body is an ongoing process which increases and decreases depending on the true need of the body for insulin from the outside, as judged by the blood sugar level at any moment of the day or night.

The concept of an artificial pancreas is a composite of the following three components:

The first component is a miniaturized device to be implanted in the body which will constantly measure the level of glucose in the blood or tissues. The second component would be an implanted storage and release device which is filled with insulin, and which can be refilled occasionally with insulin from the outside with the aid of a syringe. A third component would be a miniaturized computer element which is plugged in between the glucose sensor and the insulin providing reservoir. Whenever the glucose sensor senses that the normal blood or tissue or glucose level is being exceeded, i.e., that the body needs additional insulin, it would send an electric signal to the modulating computer. The latter, in turn, would send an appropriate electronic signal to the reservoir to release an appropriate amount of insulin into the bloodstream. Thus if there is need for extraneous insulin, the body would receive it automatically as the need is being sensed from minute to minute. When there is no further need for the supply of insulin, the computer would shut down the release of insulin from the reservoir until rising blood glucose levels activate the mechanism again.

This concept of a small, implantable artificial organ is designed to imitate the divine prototype—the natural beta-cell of the pancreas which stores and releases insulin on the basis of natural impulses conducting to it. There are two groups in this country working to reduce this concept to actual practice: the well-known Joslin Clinic in Boston and a group of scientists in Southern California. There are, however, a great many problems which still must be solved before this concept of an artificial organ can actually become reality.

TRAINING PROGRAMS

Mr. Conte. Aside from direct training, what is your estimate of the general contribution of the old training program to research? In other words, do you have any documentation of research contributions from those programs?

Dr. Lamont-Havers. When you put it that way, research contributions, it would indicate the fact that it was contributions made by the fellow or trainee while supported by this Institute. Indeed, what we would have to do is see what happened to those individuals in the rest of their career, because obviously we were supporting them very early in their career at which time they were learning techniques and concepts.

What we can do really is to look back at the particular field such as arthritis and dematology, gastroenterology, orthopedics, and see how those fields or disciplines or specialties have improved over the last 15 years in the investigative medicine which they have undertaken, the research which has been coming out under that aegis.

Take dermatology for instance. I think one of the great things which we can attribute to the training program is the lifting of dermatology into the 20th Century. Now dermatology has a number of very brilliant clinical investigators who are really pushing forward the frontiers of that specialty. All you have to look at is what the record of dermatology was when I went to school. They slapped on ointment and that was was everything.

That is clearly the result of our training programs of NIH. So when you say "specific", we can point to the whole development of the field, and in arthritis the same way really.

ARTHRITIS

Mr. CONTE. Will you put in the record some examples of progress and breakthroughs on arthritis?

Dr. LAMONT-HAVERS. Yes.

[The information follows:]

(CLERK'S NOTE: A special report on arthritis can be found on page 416.)

TRANSPLANTATION REJECTION

Mr. CONTE. Can you foresee any possible breakthroughs soon on transplantation rejection?

Dr. LAMONT-HAVERS. I think that the amount of information which is accruing as to the complex immunological reactions which are involved is expanding at enormous rates, and we would certainly expect that. When you say soon I wouldn't expect that in the next year or two but I think a little further off.

I think too frequently we try to say next year is going to be the year. Biomedical research doesn't quite work out the secrets of disease that fast. We certainly know a great deal, and certainly when we look at what happened in the kidneys, kidney transplants are lasting much, much longer.

With respect to the other organs, I think that knowledge is gaining. When we can actually say, "Yes, we can put in any organ and it is going to stay there," I am not quite sure that is going to be for another few years.

COOLEY'S ANEMIA

Mr. CONTE. How long does it generally take before there is a dangerous iron buildup in blood transfusions from Cooley's anemia?

Dr. LAMONT-HAVERS. This usually takes a number of years, 5 to 10 years, before that happens. Usually the transfusions start in early childhood, five or before, and usually the patients are in serious condition by the time they are in their late teens or early twenties. It is from that which they usually die, the complications of the iron buildup.

Mr. CONTE. I don't know whether this is one of Congressman Giaimo's questions, but for the record will you provide a project-by-project list of what you are now funding on Cooley's anemia and also list any such projects approved but not funded in 1973 and so far in 1974?

Dr. LAMONT-HAVERS. Yes.

[The information follows:]

EXTRAMURAL RESEARCH PROJECTS RELATING TO COOLEY'S ANEMIA SUPPORTED BY NIAMDD ACTIVE AS OF MAR. 29, 1974

Principal investigator and institution	Title of project	Current direct support
John F. Bertles: St. Lukes Hospital Center, New York, N.Y.	Genetic control of hemoglobin synthesis	$45,496
Prawase Wasi: Siriraj Hospital, Bangkok, Thailand	Thalassemias, hemoglobinopathies, related problems (G6PD).	15,000
Robin M. Bannerman: Research Foundation SUNY, Buffalo, N.Y.	Abnormalities of hemoglobin metabolism	34,537
Paul Saltman: University of California, San Diego, Calif.	Studies on biological transport mechanisms	41,262
Ronald Rieder: Research Foundation, SUNY, Downstate, N.Y.	Protein synthesis in erythroid precursors	45,351
George Honig: University of Illinois, Chicago, Ill.	Regulation of hemoglobin synthesis	19,770

EXTRAMURAL RESEARCH PROJECTS RELATING TO COOLEY'S ANEMIA SUPPORTED BY NIAMDD ACTIVE AS OF MAR. 29, 1974—Continued

Principal investigator and institution	Title of project	Current direct support
Edward Burka: Thomas Jefferson University, Philadelphia, Pa.	Biochemical determinants of RBC differentiation.	$33,119
Vernon Ingram: Massachusetts Institute of Technology, Cambridge, Mass.	Differentiation and immuniology of erythropoiesis.	69,982
Haig Kazazian: Johns Hopkins Hospital, Baltimore, Md	The genetic control of hemoglobin	23,456
Martha Fedorko: Rockefeller University, New York, N.Y	Iron storage and mobilization	17,593
Sherman Weissman: Yale University Medical Center, New Haven, Conn.	Hemoglobin mRNA in thalassemia	13,271
Philip Aisen: Albert Einstein College of Medicine, New York, N.Y.	Iron-binding proteins and control of iron metabolism.	57,233
David Nathan: Childrens Hospital Medical Center, Boston, Mass.	Molecular basis of thalassemia	62,041
David W. Smith: Northwestern University, Evanston, Ill	Transfer RNA and hemoglobin synthesis	18,511
Francesco Conconi: University of Ferrara, Ferrara, Italy	Molecular pathology of beta-thalassemia	11,100
Elias Schwartz: Childrens Hospital, Philadelphia. Pa	Hemoglobin synthesis in infants and children	44,681
Peter Rowley: University of Rochester, Rochester, N.Y	Hemoglobin synthesis in thalassemia	40,774
John Nielands: University of California, Berkeley, Calif	Chelates for Cooley's anemia	42,552
Helen Ranney: University of California, San Diego, Calif	Studies of the properties of hemoglobin	71,947
Total, direct cost (19)		707,676
Estimated indirect costs		242,733
Total, active as of Mar. 29, 1974 (19)		950,409

Of the five research grant applications originally reported as approved but unfunded in 1973, one project will now be funded as a result of the release of 1973 impounded funds, and one application was a supplemental request for an additional technician for an ongoing grant rather than a total project which was unfunded.

The remaining three applications representing about $127,000 are truly unfunded. However, when compared to the 22 awards for over $992,000 which were made in 1973, this gives a funding rate of over 88% which is at least twice as high a rate of funding as other programs funded by the National Institute of Arthritis, Metabolism, and Digestive Diseases.

DIABETES AND CARDIOVASCULAR DISORDERS

Mr. CONTE. Do you have any clues as to why diabetes seems to remove the relative immunity of women to heart attacks?

Dr. LAMONT-HAVERS. I wish we did have more information on this whole question of the complications of diabetes. Certainly that relating to the cardiovascular involvement is one of high priority. The small blood vessel involvement is one of the most serious complications of diabetes. Why that occurs is obviously one of the areas both this Institute and the Heart Institute are working on quite extensively.

Mr. CONTE. You mention the Heart Institute. Do you have liaison between yourself and the other Institutes?

Dr. LAMONT-HAVERS. Very close.

Mr. CONTE. All of the Institutes?

Dr. LAMONT-HAVERS. It depends on what disease. In diabetes for instance we have liaison with the Heart Institute and Eye Institute, which are the two primary ones involved after our Institute. In Cooley's anemia we spread across the Institutes. In Cooley's anemia and related diseases the Arthritis and Heart Institutes are having joint cooperative programs to make sure we are coordinating our efforts in that area.

As you can see, we are beginning to utilize the mechanism of coordination of activities between the Institutes more and more.

Mr. CONTE. That is encouraging to hear.

Dr. LAMONT-HAVERS. I certainly think the Cooley's Anemia Act did stimulate us to do this in Cooley's anemia. This has proven to be very successful. We are now really beginning to make sure that we have done that properly in diabetes also.

Mr. CONTE. Thank you, Mr. Chairman.

Mr. FLOOD. Mr. Patten.

Mr. PATTEN. Thank you, Mr. Chairman.

DIABETES

I notice the Institute completed plans to permit support of diabetes research centers throughout the United States in the next year or two. That is good news.

Dr. LAMONT-HAVERS. Yes, sir. We will be funding four such centers this year.

ARTHRITIS

Mr. PATTEN. I couldn't help but note, without being critical, that in the field of arthritis you state, "Their individual causes are as yet not known."

Dr. LAMONT-HAVERS. Right.

PSORIASIS

Mr. PATTEN. Then we turn to psoriasis, you also state, "The absence of a cure or safe remedy."

We turn to sugar diabetes and you say, "The complicated disease for which there is no known cure."

I guess all of us during our lifetime have had 10,000 theories from lay people.

Dr. LAMONT-HAVERS. A number.

Mr. PATTEN. I had a doctor who was raised in Hungary, and he is as good a man as there is in New York today, state that the Hungarians have a lot of psoriasis. His theory was that you find in those cases a relationship with fatty substances, more like a nutrition problem.

In your statistics throughout the world—are there any other indicators on diabetes or arthritis that seem to hold any promise?

ARTHRITIS

For instance, wouldn't there be more arthritis 1,000 miles further north in the cold areas than there would be in Florida or there would be in tropical countries?

Dr. LAMONT-HAVERS. No. One of the areas that the Institute has been particularly interested in are population studies in arthritis. Particularly rheumatoid arthritis and spondylitis. We have found that in certain native Indians, our southwest Indians and the Haida Indians off the British Columbia coast and Alaska, have a much higher incidence—the Pimas of rheumatoid arthritis, the Haida of spondylitis—than the general population throughout the world.

In other countries, in Russia for instance, they find that the incidence of rheumatoid arthritis in their northern population is the same as their incidence in the southern population and is the same as ours. They have some difference with regard to the severity of the disease. Thus, there doesn't seem to be any difference as far as climate is concerned. The geographic locations may be related to severity in some cases. As in the Pimas, some genetic makeup may be important. We don't know what that means. This is one of the things which we are studying.

In some of the arthritic diseases, particularly in spondylitis and in some of the related rarer diseases, there are some genetic differences showing up with regard to certain antigens which occur on the white blood cells which are really fascinating. At this time last year we were just beginning to start to study this phenomenon. Interestingly enough the Pima Indians also have a higher incidence of diabetes and a higher incidence of gall bladder disease. So they in turn are a fascinating group of people to study.

Dr. STONE. Mr. Patten. each one of the Institutes has a unit in what we call epidemiology. This will be of interest to you because the members of the committee have from time to time sought clues as to why the incidence of certain diseases is different in different population groups and from one country to another. Each one of the Institutes is energetically pursuing those kinds of clues, and in many cases they are providing us with some new approaches to research. They are often extremely exciting and interesting.

Mr. PATTEN. That is what I wanted to know.

I don't have to tell you, you put 30 years of your life in arthritis, at least 30, and yet you write here that there really is no cure. That is my impression.

Dr. LAMONT-HAVERS. There is no cure.

PSORIASIS

Mr. PATTEN. You say there are 6 million with psoriasis. I believe it; I see it.

Dr. STONE. It is very difficult to measure the economic impact of a disease.

Mr. PATTEN. You said a million. You are very modest. You know they can't pass physical exams for the draft. You said there is no compensation. I know that and I have seen severe cases so that people would shy away and change their life. You state that probably some turn to alcoholism and other outlets, suicides.

I had a tough one on diabetes. A fellow 35 went blind making about $25,000 a year as an engineer. There was a happy ending. We sent him out to our Government computer training plant for the blind in Cincinnati. and now he is working on computers, and I know the people around him tell me he is one of the best. It was a terrible adjustment for that family to make. Of course it took 3 years to arrive at this point.

I see a lot of my friends are carrying canes walking with strollers I guess you call them.

If you did come up with something on these three, arthritis, diabetes, and psoriasis you would surely make millions of people happy.

You are entitled to make a breakthrough on one of these subjects with all we know about chemistry and all the other technology. You put in 40 years. What do you recommend to a fellow at age 70 with a couple of bum knees and not getting around? You are not going to tell him to go to Arizona?

Dr. Lamont-Havers. It would all depend on who he was and who he had in Arizona and what he would like to do down there. It is quite likely he could get worse in Arizona. I have told a lot of patients to go to Arizona, and I have told an awful lot not to depending on their particular circumstance.

When we look at the type of research we are doing, and I look at the research I was doing in the early fifties in rheumatoid arthritis, at that time it seemed very sophisticated and very advanced. Yet now, 15 years later, that was the most unsophisticated, naive type of thing when we look at the advances in the same area I was working on during that time. This 15- or 20-year span, which is really the era of the great exploding of knowledge helped by the support of NIH and this Congress is not a very long time in the history of man. It is just not even a blink. It takes a long time to crack the secrets of nature.

I think we should be pleased with the advances we have made in 20 years, but to think that we could get the answer to these things quickly was very naive. Diabetes seems to be becoming more complex everyday. I mentioned in my statement the discovery of somatostatin in the brain. Even since this statement was written we are beginning to realize that this substance released from the hypothalamus plays a part in diabetes which we never would have suspected before.

Mr. Patten. On psoriasis I have heard doctors say people who work for a living don't have it.

Dr. Lamont-Havers. That is not true.

Mr. Patten. I have heard it said though by good men. I can never check it out.

I have a little theory of my own.

Every summer at least I just thought maybe the acid and perspiration was enough to dissolve the salts, and if we all did more work we wouldn't have psoriasis.

Dr. Lamont-Havers. It is the sunlight, the ultraviolet light.

Mr. Patten. You have millions of people out there with one of these three troubles. If you came up with something, you would be a hero.

Mr. Chairman, that is all.

Mr. Flood. Mr. Conte.

ARTHRITIS FOUNDATION

Mr. Conte. Take the Arthritis Foundation. How much do they raise for research?

Dr. Lamont-Havers. The Arthritis Foundation is now raising somewhere between $8 million and $10 million per year and I am not quite sure exactly.

Mr. Conte. Do they work separately? I should know this but I don't. Do they work with you or take that $8 million and work on their own?

Dr. Lamont-Havers. I used to be the medical director of the Arthritis Foundation and obviously we maintain a very close liaison with that group. And the fellowship program supported by the foundation has indeed been a major factor in helping to bring people into the field of arthritis. It really has. Our training programs and their fellowship programs, have really worked side by side and dovetailed very well. Now with the phaseout of the training programs this puts a terrific strain on their resources.

Mr. CONTE. Will they pick it up?

Dr. LAMONT-HAVERS. Unfortunately they can't pick it up. They are trying to.

Mr. FLOOD. Thank you very much.

Dr. LAMONT-HAVERS. Thank you.

[Justifications follow:]

JUSTIFICATION OF THE BUDGET ESTIMATES

NATIONAL INSTITUTES OF HEALTH

National Institute of Arthritis, Metabolism, and Digestive Diseases

Amounts Available for Obligation

	1974 Revised	1975
Appropriation	$159,447,000	$152,961,000
Amount withheld (PL 93-192)	6,486,000	---
Subtotal, adjusted appropriation	152,961,000	152,961,000
Real transfer to:		
"Departmental Management" (For Department-wide reductions in public affairs)	-20,000	---
Comparative transfer to:		
"Office of Assistant Secretary for Health" (Transfer of administrative support activities to the Office of the Assistant Secretary for Health)	-63,000	---
"Departmental Management" (Transfer of accounting functions from the OS Working Capital Fund)	-8,000	---
Comparative transfer from:		
"Departmental Management" (Transfer of indirect cost negotiation function to the OS Working Capital Fund)	10,000	---
"National Institute of General Medical Sciences" (Decentralization of scientific evaluation grants program)	256,000	---
Subtotal, budget authority (base obligations)	153,136,000	152,961,000
Unobligated balance, restored	24,530,000	---
Comparative transfer of restored unobligated balance to Research Resources for General Research Support Grants	-6,179,000	---
Total, obligations	171,487,000	152,961,000

Summary of Changes

1974 Estimated obligations	$171,487,000
1975 Estimated obligations	152,961,000
Net change	-18,526,000

	1974	Change from 1974
Increases:		
A. Built-in:		
1. Within-grade pay increases	---	+202,000
2. Annualization of pay increases	---	+140,000
3. One extra day of pay in 1975	---	+37,000
4. Bureau of Employee Compensation	---	+4,000
5. Services and Supplies	---	+277,000
6. Payment to NIH management fund	---	+358,000
Subtotal	---	+1,018,000
B. Program:		
1. Research grants:		
a. Noncompeting continuations	$67,838,000	+18,195,000
b. Competing (new, continuations, and supplementals)	45,199,000	+33,916,000
c. Scientific evaluation	256,000	+44,000
d. Multidisciplinary centers	---	+4,000,000
2. Fellowships:		
a. Noncompeting continuations	500,000	+2,000,000
b. Competing (new, continuations, and supplementals)	3,122,000	+2,000,000
3. Research and development contracts	7,649,000	+826,000
Subtotal	---	+60,981,000
Total, increases	---	+61,999,000

Summary of Changes -- continued

	1974	Change from 1974
Decreases:		
A. Built-in:		
1. Annualization of employment savings......................	---	-$37,000
Subtotal.....	---	-37,000
B. Program:		
1. Research grants:		
a. Noncompeting completed or converted to competing status..................	$67,838,000	-16,953,000
b. Competing completed or converted to noncompeting.	38,952,000	-38,952,000
c. 1974 obligations used to fund 1975 continuations...	6,247,000	-6,247,000
d. Research career program.....	3,406,000	-1,225,000
2. Fellowships:		
a. Noncompeting completed or converted to competing status..................	500,000	-477,000
b. Competing completed or converted to noncompeting.	3,122,000	-3,122,000
3. Training grants:		
a. Noncompeting completed......	12,696,000	-11,190,000
b. Competing completed.........	2,322,000	-2,322,000
Subtotal.....	---	-80,488,000
Total, decreases.........	---	-80,525,000
Total, net change.........................	---	-18,526,000

Explanation of Changes

Increases:

A. Built-in:

These increases will provide $202,000 for within-grade pay increases, $140,000 for annualization of 1974 pay increases, $37,000 for one extra day of pay in 1975, $4,000 for increased payment to the Bureau of Employee Compensation, $277,000 for increased costs of supplies and services, and $358,000 for this Institute's proportionate share of increased costs of the National Institutes of Health Management Fund for centrally furnished services such as patient care, receipt and initial review of all grant applications, computer services, maintenance of buildings and grounds, custodial services, communications, and transportation.

B. Program:

1. Research grants:
   - a. The increase of $18,195,000 in noncompeting research grants represents the continuation of previously awarded grants plus "new" continuations resulting from grants made in 1974. The number of continuations increased by 18: from 1,135 in 1974 to 1,153 in 1975.
   - b. The amounts of $33,916,000 in competing research grants reflects: (a) $18,250,000 for 277 new awards; (b) $15,166,000 for 212 competing continuations and (c) $50,000 for 42 supplementals.
   - c. The increase of $44,000 for scientific evaluation represents this Institute's proportionate share of the increased costs related to the initial review and evaluation of research grant applications.
   - d. The $4,000,000 increase for multidisciplinary centers includes $2,000,000 for regional research centers in diabetes and related metabolic and endocrine disorders, and $2,000,000 for a regional centers program to conduct research and clinical investigations in gastroenterology and nutrition.

2. Fellowships:
   - a. The increase of $2,000,000 in noncompeting fellowships represents the continuation of previously awarded grants plus "new" continuations resulting from grants made in 1974. The number of continuations increased by 99: from 56 in 1974 to 155 in 1975.
   - b. The amount of $2,000,000 in competing fellowships represents 160 new Research Training fellowships.

3. Research and development contracts:
   - a. The increase of $826,000 for research and development contracts will support new efforts in the areas of arthritis, skin diseases, diabetes and endocrinology, digestive diseases, kidney diseases and Cooley's anemia.

Decreases:

A. Built-in:

This decrease represents the annualization of savings related to the reduction of 30 positions in 1974.

Explanation of Changes -- continued

B. Program:

1. Research grants:
   a. The decrease of $16,953,000 represents 274 noncompeting regular research grants that were completed in 1974 or that are being converted to competing status in 1975.
   b. The decrease of $38,952,000 reflects the completion or conversion to a noncompeting status of 587 competing grants.
   c. The decrease of $6,247,000 reflects the reduced funding required in 1975 due to the multi-year funding of 111 projects in 1974.
   d. The decrease of $1,225,000 reflects the completion of 47 research career awards.

2. Fellowships:
   a. The decrease of $477,000 reflects the completion of 54 noncompeting fellowships.
   b. The decrease of $3,122,000 represents the completion or conversion to noncompeting status of 286 competing fellowships.

3. Training grants:
   a. The decrease of $11,190,000 reflects the completion of 136 noncompeting training grants.
   b. The decrease of $2,322,000 reflects the completion of 46 competing training grants.

Obligations by Activity

Page Ref.		1974 Base *		1975 Estimate		Increase or Decrease		
		Pos.	Amount	Pos.	Amount	Pos.	Amount	
180	Arthritis, Bone and Skin Diseases.....	---	$23,530,000 (27,037,000)	---	$22,379,000	---	-$1,151,000	A
183	Diabetes, Endocrinology and Metabolism........	---	46,197,000 (52,968,000)	---	46,858,000	---	+661,000	B
189	Digestive Diseases and Nutrition.....	---	26,009,000 (30,301,000)	---	26,650,000	---	+641,000	C
193	Kidney Diseases.....	---	18,121,000 (20,201,000)	---	17,335,000	---	-786,000	D
197	Hematology..........	---	11,039,000 (12,740,000)	---	10,518,000	---	-521,000	E
200	Intramural Laboratory and Clinical Research.	451	22,484,000	451	23,313,000	---	+829,000	F
205	Research Management and Program Services..	106	5,756,000	106	5,908,000	---	+152,000	G
	Total obligations (bases).............	557	153,136,000	557	152,961,000	---	-175,000	
	Total obligations.......		(171,487,000)					

* 1974 Base - Excludes 1973 appropriation restorations. Total obligations shown in parentheses.

Explanation of Changes (by Activity)

A. The net decrease for the Arthritis, Bone and Skin Diseases Program includes an increase of $1,084,000 for research activities. Specific program plans relate to the development of new biomaterials for surgically implantable artificial joints and to the new US-USSR cooperative program in arthritis. This increase is offset by a decrease of $2,235,000 for training activities.

B. The net increase for the Diabetes, Endocrinology and Metabolism Program includes an increase of $3,477,000 for research activities such as expansion of the program for regional research centers, synthesis of insulin, transplantation of insulin producing cells and development of standard immunoassay resources for endocrine studies. This increase is offset by a decrease of $2,816,000 for training activities.

C. The net increase for Digestive Diseases and Nutrition includes an increase of $2,435,000 for research activities with specific emphasis on the development of the regional centers program to conduct research and clinical investigations in gastroenterology and nutrition aimed at better diagnosis and treatment and eventual prevention of the various disease entities in these areas. This increase is offset by a decrease of $1,794,000 in training activities.

D. The net decrease of $786,000 for the Kidney Disease Program includes $325,000 for research activities particularly the initiation of a new program to give additional emphasis in the prevention, diagnosis and treatment of diseases of the kidneys and urologic tract. This increase is offset by a decrease of $1,111,000 for training activities.

E. The net decrease in the Hematology Program includes an increase of $672,000 for research activities with special emphasis on the exploration of new initiatives in Cooley's Anemia. This increase is offset by a decrease of $1,193,000 for training activities.

F. and G. The increases in both of these activities are required for mandatory items primarily including annualization of the cost of recent pay increases and an increase of this Institute's proportionate share of increased costs of centrally furnished services such as patient care, receipt and initial review of all grant applications, computer services, maintenance of buildings and grounds, custodial services, communications, and transportation.

Obligations by Object

	1974 Estimate	1975 Estimate	Increase or Decrease
Total number of permanent positions	557	557	---
Full-time equivalent of all other positions	51	55	+4
Average number of all employees	615	610	-5
Personnel compensation:			
Permanent positions	$10,691,000	$10,669,000	-$22,000
Positions other than permanent	516,000	564,000	+48,000
Other personnel compensation	55,000	58,000	+3,000
Subtotal, personnel compensation	11,262,000	11,291,000	+29,000
Personnel benefits	1,269,000	1,267,000	-2,000
Travel and transportation of persons	250,000	250,000	---
Transportation of things	56,000	56,000	---
Rent, communications and utilities	400,000	450,000	+50,000
Printing and reproduction	160,000	160,000	---
Other services	12,242,000	13,044,000	+802,000
Projects contracts	7,162,000	8,475,000	+1,313,000
Supplies and materials	1,851,000	1,853,000	+2,000
Equipment	750,000	850,000	+100,000
Grants, subsidies and contributions	136,085,000	115,265,000	-20,820,000
Total obligations by object	171,487,000	152,961,000	-18,526,000
Total obligations excluding 1973 appropriation	153,136,000		

Significant Items in House and Senate Appropriations Committee Reports

Item	Action taken or to be taken
1974 House Report	
1. "Increased emphasis should be placed on digestive disease research, especially gallstone research, and the further development of endoscopy..." (Page 33).	1. Of the additional funds provided by Congress, nearly 20% have been allocated to the area of digestive diseases. Plans are being made for a program to develop endoscopes through research and development contract mechanism.
1974 Senate Report	
1. "The Committee recommends that a portion of the total increase... be used for this purpose" [development of new gallstone therapy] (Page 47).	1. (See House Report above).
2. "The Committee recommends that increased resources be made available for this purpose" [development of endoscopy] (Page 47-48).	2. (See House Report above).
3. "The Committee has provided additional funds for the establishment of Diabetes Centers throughout the Nation...." "It is felt that there should be programs on an inter-Institute basis..." and "The Committee recommends that the director of the NIAMDD create a position for an associate director for diabetes who would chair the Inter-Institute Committee." (page 47).	3. Of the additional funds made available to the Institute in 1974, over $2,000,000 has been allocated to the diabetes program. An Inter-Institute Committee is being established.
4. "The Committee has provided increased funds and positions to accelerate this program" [the Artificial Kidney-Chronic Uremia Program] (Page 47).	4. An increase of $500,000 over the amount in the Budget request has been allocated to this program in 1974.
5. "In dermatology the Committee has provided for expanded research in psoriasis." (Page 47).	5. The allocation of funds for research grants in psoriasis has been increased from $550,000 to $670,000.

Item	Action taken or to be taken
1974 Senate Report--continued	
6. "The Committee therefore calls the National Institutes of Health to give special attention to arthritis and diabetes research in its allocation of research grants in 1974." (Page 48).	6. Of the additional funds made available to the Institute in 1974, over $1,300,000 has been allocated for research grants in arthritis and and over $2,000,000 has been allocated for research grants in diabetes.
1974 Conference Report	
1. "The conferees urge the NIH to establish mechanisms to assure a coordinated program of research by the Institutes concerned with the various aspects of diabetes." (Page 23).	1. (See Senate Report, Item 2 above).

Authorizing Legislation

Legislation	1975 Authorization	 Appropriation Requested
Public Health Service Act Section 301--Research and Investigation, in general	Indefinite	
		$152,961,000
Title IV, Part D--National Institute on Arthritis, Metabolism, and Digestive Diseases	Indefinite	

National Institute of Arthritis, Metabolism, and Digestive Diseases

Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
1965	113,369,000	113,344,000	113,544,000	113,344,000
1966	119,203,000	121,203,000	123,203,000	123,203,000
1967	129,908,000	133,687,000	135,687,000	135,687,000
1968	143,954,000	143,954,000	147,204,000	143,954,000
1969	151,718,000	141,287,000	147,287,000	143,888,000
1970	137,668,000	137,668,000	155,000,000	146,619,000
1971	132,152,000	138,339,000	140,339,000	138,339,000
1972	135,594,000	148,365,000	163,790,000	153,164,000
1973 *	131,857,000	158,307,000	172,991,000	158,307,000*
1974	133,783,000	156,069,000	163,175,000	159,622,000**
1975	152,961,000			

NOTES:

* This appropriation authority was the continuing resolution. The appropriation amount was the House Allowance, which was the lower of the House or Senate amounts in the first vetoed bill.

**	Appropriation after reduction	153,136,000

Justification

National Institute of Arthritis, Metabolism, and Digestive Diseases

Authorizing Legislation: Public Health Service Act Title IV Part D

	1974 Base *		1975		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits.........	551	$12,531,000	551	$12,548,000	---	+$17,000
Other expenses.........	---	140,605,000	---	140,413,000	---	-192,000
Total.........	551	153,136,000	551	152,961,000	---	-175,000

* Excludes 1973 appropriation restorations.

General Statement

The National Institute of Arthritis, Metabolism, and Digestive Diseases (NIAMDD) conducts, fosters, and assists research and training directed toward preventing, diagnosing, treating and controlling the numerous diseases and disorders within its purview. Research and training projects are supported in over 400 non-Federal institutions through the use of grants and contracts, the vast majority of which are awarded to universities and medical schools. Approximately 93% of the funds in these program categories are used for grants and 7% are used for contracts. In addition, the Institute conducts intramural research and clinical research projects at facilities at the National Institutes of Health in Bethesda, Maryland and at field stations in Phoenix, Arizona.

Research grant applications, initiated by the investigator, are reviewed on scientific merit and within the available funds, compete on this basis with other applicants in the same program area. Approximately 490 applicants in 1974 and 489 in 1975 will receive awards from current year funds and will be promised support for an average of two additional years. When these awards are combined with those awards made in prior years which are continuing as a result of a commitment for future support, the Institute will be supporting approximately 1,625 individual research projects in 1974 and estimates it will support a total of 1,642 projects in 1975.

Research and development contracts are also awarded as the result of competition based on scientific merit. Proposals, in this case, however, are solicited in response to specific, well defined objectives developed by the Institute to meet special needs in the development of program objectives.

When the need becomes evident for new development, such as new, more efficient, less costly artificial kidney machines or coordinated clinical evaluation of the efficacy of various regimens in the treatment of regional ileitis, it is usually impractical and inefficient to reassign intramural scientists who have specialized and are engaged in a productive research program. It is likewise seldom that competent outside scientists will volunteer to drop their ongoing studies in favor of a new problem which has become a special programmatic interest to the Institute. In attempting to meet special needs, direct collaboration is sought with special scientific talent or resources, usually already engaged and competent in closely related efforts and techniques, through the use of research and development contracts.

In addition to universities and medical schools, both non-profit and commercial research organizations may be awarded contracts. In 1974 approximately 73 contracts will be awarded for a one year period, although future support may be planned. In 1975 approximately 83 contracts will be supported.

Previously supported programs supporting research training will be phased out after all current commitments to trainees for fellowships and training grants have been fulfilled. In their place a new program is being initiated to provide for post-doctoral training in specific shortage areas in biomedical and health-related sciences only. The program is directed toward the training of individuals for full-time careers in research and/or teaching. Upon completion of their training, recipients are expected to pursue this objective for a period at least as great as the period of training and individuals who go into clinical medicine or non-health related research may be required to reimburse the Government for the cost of the training.

Under this new program, the Institute expects to make 160 awards in 1974 and to double that number to 313 in 1975.

The mission of the intramural research area of the Institute is to obtain information and knowledge for the understanding of the fundamental biological processes underlying the major diseases within the Institute's purview. Over 260 research projects including various combinations of laboratory, clinical, epidemiological and biometric investigations are conducted in facilities in Bethesda, Maryland and Phoenix, Arizona. Medical, biological, physical and chemical investigations range from studies of fundamental mechanisms, to specific disease oriented laboratory research, to clinical evaluation and treatment programs. Close collaboration with scientists of other NIH Institutes, other government agencies and outside investigators ensure a minimum of duplication and a maximum exchange of research findings.

DHEW - National Institutes of Health

CROSSWALK - 1974 COLUMN 1975 PRESIDENT'S BUDGET

NATIONAL INSTITUTE OF ARTHRITIS, METABOLISM, AND DIGESTIVE DISEASES
(Amounts in thousands)

	Research Grants								
		Specials		Training Programs					
Program	Regular Program	Multi-disciplinary Centers	Other	Grants	Fellowships	Laboratory and Clinical Research	Research and Development Contracts	Other Direct Operations	Total
1974 Base Obligations									
1. Arthritis, Bone and Skin Diseases..................	$19,383		$498	$2,955	$644		$50		$23,530
2. Diabetes, Endocrinology and Metabolism................	39,226		1,767	3,424	1,035		745		46,197
3. Digestive Diseases and Nutrition.................	20,292		853	2,208	546		2,110		26,009
4. Kidney Diseases................	12,362		223	1,503	364		3,669		18,121
5. Hematology....................	8,619		321	1,606	393		100		11,039
6. Intramural Laboratory and Clinical Research............						$22,484			22,484
7. Research Management and Program Services.............								$5,756	5,756
Subtotal..................	99,882		3,662	11,696	2,982	22,484	6,674	5,756	153,136
Unobligated Balance Restored									
1. Arthritis, Bone and Skin Diseases.................	2,535		52	840	80				3,507
2. Diabetes, Endocrinology and Metabolism................	5,226		105	972	293		175		6,771
3. Digestive Diseases and Nutrition.................	2,640		52	627	173		800		4,292
4. Kidney Diseases................	1,594		25	427	34				2,080
5. Hematology....................	1,160		25	456	60				1,701
6. Intramural Laboratory and Clinical Research............									0
7. Research Management and Program Services.............									0
Subtotal..................	13,155		259	3,322	640		975		18,351
Total Obligations.................	113,037		3,921	15,018	3,622	22,484	7,649	5,756	171,487

DHEW - National Institutes of Health

CROSSWALK - 1975 COLUMN 1975 PRESIDENT'S BUDGET

NATIONAL INSTITUTE OF ARTHRITIS, METABOLISM, AND DIGESTIVE DISEASES
(Amounts in thousands)

	Research Grants								
		Specials		Training Programs					
Program	Regular Program	Multi-disciplinary Centers	Other	Grants	Fellowships	Laboratory and Clinical Research	Research and Development Contracts	Other Direct Operations	Total
1. Arthritis, Bone and Skin Diseases................	$20,025		$290	$341	$1,023		$700		$22,379
2. Diabetes, Endocrinology and Metabolism................	40,484	$2,000	1,486	443	1,200		1,245		46,858
3. Digestive Diseases and Nutrition.................	20,539	2,000	641	360	600		2,510		26,650
4. Kidney Diseases................	12,659		50	156	600		3,870		17,335
5. Hematology....................	9,289		273	206	600		150		10,518
6. Intramural Laboratory and Clinical Research.............						$23,313			23,313
7. Research Management and Program Services..............								$5,908	5,908
Total Obligations..................	102,996	4,000	2,740	1,506	4,023	23,313	8,475	5,908	152,961

National Institute of Arthritis, Metabolism, and Digestive Diseases

Budget Mechanism

	1974*		1975	
	Number	Amount	Number	Amount
Grants				
Regular				
Non-competing....................	1,135	$67,838,000	1,153	$69,080,000
Competing........................	368	17,922,000	277	18,250,000
New..............................	122	13,722,000	212	15,166,000
Supplemental.....................	(34)	400,000	(42)	500,000
Subtotal.........................	1,625	99,882,000	1,642	102,996,000
Special				
Multi-disciplinary centers.......	---	---	---	4,000,000
Research career programs........	---	3,406,000	---	2,440,000
Scientific evaluation...........	---	256,000	---	300,000
Subtotal.........................	---	3,662,000	---	6,740,000
Total Grants.....................	1,625	103,544,000	1,642	109,736,000
Fellowships				
Non-competing....................	56	500,000	155	2,023,000
Competing........................	6	52,000	---	---
New..............................	209	2,430,000	160	2,000,000
Supplemental.....................	---	---	---	---
Subtotal.........................	271	2,982,000	315	4,023,000
Training Grants				
Non-competing....................	175	11,696,000	39	1,506,000
Competing........................	---	---	---	---
New..............................	---	---	---	---
Supplemental.....................	---	---	---	---
Subtotal.........................	175	11,696,000	39	1,506,000
Laboratory & Clinical Research......		21,245,000		22,064,000
Research & Development Contracts....		6,674,000		8,475,000
Biometry, Epidemiology, & Field Studies.....................		1,239,000		1,249,000
Research Management & Program Services........................		5,756,000		5,908,000
TOTAL............................		153,136,000		152,961,000

* Excludes 1973 appropriation restorations.

Arthritis, Bone and Skin Diseases

Authorizing Legislation: Public Health Service Act Title IV Part D

	1974 Base *		1975		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits.........	---	---	---	---	---	---
Other expenses.........	---	$23,530,000	---	$22,379,000	---	-$1,151,000
Total.........	---	23,530,000	---	22,379,000	---	-1,151,000
Subactivities:						
Arthritis............	---	11,740,000	---	11,593,000	---	-147,000
Bone Diseases........	---	7,240,000	---	7,076,000	---	-164,000
Skin Diseases........	---	4,550,000	---	3,710,000	---	-840,000
Total.........	---	23,530,000	---	22,379,000	---	-1,151,000
Budget Mechanism:						
Research Grants:						
Regular............	---	19,383,000	---	20,025,000	---	+642,000
Special............	---	498,000	---	290,000	---	-208,000
Subtotal.........	---	19,881,000	---	20,315,000	---	+434,000
Fellowships..........	---	644,000	---	1,023,000	---	+379,000
Training Grants......	---	2,955,000	---	341,000	---	-2,614,000
Research & Development Contracts...........	---	50,000	---	700,000	---	+650,000
Total.........	---	23,530,000	---	22,379,000	---	-1,151,000

* Excludes 1973 appropriation restorations.

Arthritis & Related Diseases

The major aims of the arthritis program are to define fully the diseases which fall into this category in terms of their respective causes and complications, and to find methods for optimal treatment or prevention. This mission is fraught with great difficulty because of the diversity of the individual disorders which make up "arthritis" and the rheumatic diseases, and because, as a whole, their individual causes are as yet not known.

Future research in rheumatoid arthritis will endeavor to discover whether an infectious process, an autoimmune reaction, or possibly a combination of both processes are the mechanisms by which the disease develops. Institute grantees will continue to gather data on the possible role of microbial organisms and viruses which have recently been recognized as potential pathogens in rheumatoid arthritis in man. To date, however, firm proof that infectious agents may cause this disorder remains elusive. Researchers will also examine the possibility that rheumatoid arthritis is initiated by an autoimmune reaction, in which the body reacts abnormally and destructively to materials (perhaps released or modified by infection) originating within the body's own tissues.

Past Institute studies have contributed to control of the painful symptoms and dangerous complications of gout, but the main research objectives in this disease will continue to be the elucidation of the underlying mechanisms of the disorder and to provide a means of prevention or effective "cure."

Although the prime responsibility for acupuncture has been delegated to another Institute at the NIH, the NIAMDD is deeply interested in pursuing grant-supported investigations of acupuncture in the treatment of arthritis. Recently, the Institute co-sponsored a workshop at the NIH to review current literature on acupuncture and to study the possibility of research support in this field. The Institute will also explore the proposal for a joint US-USSR program to collaborate with Soviet rheumatologists in arthritis research.

Bone Diseases

There is no specific therapy for the treatment of osteoarthritis, another major form of arthritis. The most severe cases may require reconstructive surgery to correct deformed joints, or total replacement of nonfunctioning joints with artificial prostheses, as is being done with increasing success in the case of hip joints and knees.

Institute grantees will continue to assemble data from extensive trials of total hip replacement, employing both new and conventional materials. Ceramic materials are being compared with stainless steel, and various types of bone cements are being evaluated; these studies eventually should point to optimal procedures in hip replacement and aid in other arthritis- related surgery, as for instance knee-joint replacement.

Skin Diseases

The Institute's dermatology program is the only extramural program within the NIH that has a specific responsibility for supporting research on disorders of the skin and its appendages including hair, nails, sebaceous glands, and sweat glands. The major dermatologic diseases are: eczematous and eczematoid dermatitis; acne vulgaris, a disease of sebaceous glands; psoriasis, a hereditary disease that afflicts six to eight million Americans; fungal and bacterial infections, warts, herpes simplex, and other viral infections; disorders of the subcutaneous tissues with scleroderma and lupus erythematosus being the best known of the collagen diseases of skin; burns and their subsequent scars; abnormalities of pigment regulation causing vitiligo ("piebaldness") and also one of man's deadliest cancers -- melanoma. Pemphigus is a chronic blistering disorder of the skin and, like malignant melanoma, is ultimately fatal.

The magnitude of financial burden imposed on the six million patients with psoriasis in this country exceeds one billion dollars annually. In the absence of a cure or even of effective, safe remedies, treatments that merely ameliorate the disease are continually necessary. Patients with severe psoriasis have lost jobs, have been denied workman's compensation, have become alcoholics, and have committed suicide as a result of the social trauma and isolation imposed on individuals with this disease.

Although the etiology of psoriasis is unknown (except for some genetic influence), current information points to localized excessive epidermal cell growth as being the final tissue event that accounts for the major clinical expression of this disease; i.e., the formation of scaly lesions.

Institute-supported studies will continue to screen and develop chemotherapy agents for the topical treatment of severe psoriasis. A limited number of cytotoxic (anti-cancer) drugs will be tested on the skin of psoriatic patients for potential therapeutic effectiveness. This Institute will also initiate studies to examine the clinical implications of the recently reported low cyclic AMP levels in psoriatic skin.

Objectives in 1974 and 1975

As a result of the release of 1973 unobligated balances in 1974, approximately 40 research grants and research and development contracts, 10 fellowships and career awards and 12 training grants will be awarded.

From the new budget authority available in 1974, it is estimated that 317 research grants and research and development contracts will be awarded. As a result of the termination and phase-out of current training programs, it is estimated that 68 previously committed continuation awards will be made under the fellowship, career development award and training grant programs. In addition, approximately 10 new or competing fellowships and career development awards will be funded for either a single year or for multiple years so as not to create a continuation cost in 1975. Under the new modified Research Training Program being initiated in 1974, 40 post-doctoral M.D.'s and Ph.D.'s will be trained for careers in research and/or teaching.

Approximately 324 research grants and research and development contracts, will be awarded in 1975. The phase-out of the fellowship, career award and training grant program will be nearly completed and only 22 previously committed continuation awards will be made. The new modified Research Training Program which was initiated in 1974 will double in its second year and approximately 78 post-doctoral M.D.'s and Ph.D.'s will receive training for future careers in research or training.

A modest increase in research and development contracts will be used to provide the emphasis for this activity in 1975. Specific program plans relate to the development of new biomaterials for surgically implantable artificial joints and to the new US-USSR cooperative program in arthritis.

Diabetes, Endocrinology and Metabolism

Authorizing Legislation: Public Health Service Act Title IV Part D

	1974 Base *		1975		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits.........	---	---	---	---	---	---
Other expenses.........	---	$46,197,000	---	$46,858,000	---	+$661,000
Total.........	---	46,197,000	---	46,858,000	---	+661,000
Subactivities:						
Diabetes.............	---	9,122,000	---	10,061,000	---	+939,000
Endocrinology........	---	15,868,000	---	15,338,000	---	-530,000
Metabolism...........	---	21,207,000	---	21,459,000	---	+252,000
Total.........	---	46,197,000	---	46,858,000	---	+661,000
Budget Mechanism:						
Research Grants:						
Regular............	---	39,226,000	---	40,484,000	---	+1,267,000
Special............	---	1,767,000	---	3,486,000	---	+1,710,000
Subtotal.........	---	40,993,000	---	43,970,000	---	+2,977,000
Fellowships..........	---	1,035,000	---	1,200,000	---	+165,000
Training Grants......	---	3,424,000	---	443,000	---	-2,981,000
Research & Development Contracts...........	---	745,000	---	1,245,000	---	+500,000
Total.........	---	46,197,000	---	46,858,000	---	+661,000

* Excludes 1973 appropriation restorations.

Diabetes

A complicated disease for which there is no known cure, diabetes ranks seventh on the list of diseases causing death in the United States. Diabetes has been known for some time to be, in part, a hereditary disorder. As a result of the body's inability to metabolize carbohydrates normally, the diabetic is unable to convert carbohydrates properly into the stored form, glycogen, or to utilize them properly for the energy required for normal body functions. The carbohydrates, in the form of glucose, accumulate in the blood and overflow into the urine. As the disease progresses, abnormal carbohydrate metabolism becomes associated with a noticeable derangement in the metabolism of fats and proteins, and with changes in the cardiovascular system and in the small blood vessels of the body.

During the next fiscal year, Institute efforts will focus on attempts to define the disease in terms of its causes and the many complications associated with it, and to find methods of prevention.

Basic knowledge about diabetes still to be discovered includes the mechanism of action of insulin, a clearer understanding of the intricate details of carbohydrate and fat metabolism in the disease, and determination of the precise nature of the blood vessel abnormalities which underlie major complications of the disorder. The Institute is also concerned with exploring ways to suppress development of complications of diabetes which include enhanced atherosclerosis and consequent coronary heart disease, nerve damage, kidney failure and blindness.

The Institute has completed plans to permit support of at least one and perhaps more Diabetes-Endocrinology Research Centers throughout the United States, during the next year or two. Center grants will be limited to institutions where there is ongoing research in diabetes, and will be used to strengthen and to permit further development of these efforts. These centers will provide core resources and services at an institution where a broad and substantial volume of excellent diabetes research already exists.

The centers are conceived as providing scientific personnel, administration, and central support services to accomplish research goals that would not otherwise be achievable. The grants are not intended to give direct support for ongoing research projects. Funds to initiate projects by new investigators and for exploratory or feasibility studies may also be furnished by this mechanism. Such funds may be requested each year of the center grant, but support of any particular new project will be limited to a three-year period, at which time the project should compete for a regular research grant.

Endocrinology and Endocrine Disorders

Endocrinology concerns itself with the study of the endocrine glands and their secretions, the hormones, and with the effect of these secretions on the metabolism and physiology of man. Thus, research in the field of endocrinology is considered one of the most important areas of Institute concern.

For many years endocrinologists were concerned with the clinical conditions resulting from under or over-production of the endocrine glands. In recent years, the importance of the hormones as a control factor in the metabolism, growth and reproduction of the whole body, and particularly of the individual cells, has become more and more evident.

The Institute supports basic and clinical research on: the normal and abnormal functioning of the endocrine glands; the structure, function, and mechanism of action of the hormones produced; the effects of the hormones on various processes in the body; and the factors which contribute to the control of the effects of the endocrine system (e.g., hypothalamic secretions, prostaglandins, cyclic AMP, and others).

Most clinical symptoms of the dysfunction of endocrine glands are well-known and in most cases can be alleviated; however, not well-understood is the basis of hormonal control at the cellular level. This is important to all branches of medicine since the hormones markedly affect cellular function and the metabolism of nutrients and other cell-components. It has become apparent that the hormones act at the cellular level through a complicated system involving hormone receptors at the cell membrane, "second" intracellular messengers such as cyclic AMP, and activation of intracellular enzyme systems.

Because of the importance of knowing the precise mechanism of hormonal action on cells and tissues, NIAMDD supports many basic studies on hormone action as well as more clinically oriented investigations of the diseases caused by hormonal imbalance. The clinical studies include investigations of such abnormalities as: osteoporosis, pituitary dwarfism, acromegaly, thyroid disorders, adrenal dysfunction, and others.

Osteoporosis is a condition in which there is too little bone tissue, and bones tend to fracture as the result of minor trauma or strain. It may be caused by postmenopausal hormonal insufficiency, malfunction of the adrenals or pituitary gland, prolonged dietary calcium deficiency on skeletal disuse, and by combinations of two or more of these factors. It is quite common in postmenopausal women, who account for the majority of millions of osteoporosis patients.

Goiter is the best known of the thyroid disorders and is found in areas where there is insufficient iodine in the water or diet. Such hypothyroidism causes lethargy, slow mentation, depressed metabolism, sexual hypofunction and sensitivity to cold. Deficiency of the thyroid hormone in early life leads to cretinism. Hyperthyroidism results in a diametrically opposed clinical picture with restless overactivity, weight loss, nervousness; it may be life-threatening in severe cases. Adrenal dysfunction results in Addison's Disease (adrenal failure syndrome), Cushing's Disease (adrenal hyperfunction) and hyperaldosteronism. Fortunately these disorders are relatively rare in the population.

Probably one of the most important advances in the field of endocrinology is the elucidation by grantee-scientists during recent years of the mechanisms which serve as the bridge and controlling pathway between man's nervous system and his endocrine system. A series of compounds has been isolated, identified and synthesized, which are produced in the hypothalamus portion of the brain. These are carried to the pituitary gland to stimulate or inhibit the release of hormones which affect important body functions, from day-to-day metabolism to reproduction. Studies of these new hypothalamic hormones must be pursued vigorously in Fiscal Year 1975 since their potential for control or correction of a variety of body functions is great.

Hormone Developmental Research Program

In recent years, gradually increasing knowledge has revealed the intricate regulatory relationship between hormones and enzymes in most biochemical processes. Alteration of this relationship undoubtedly underlies the functional derangement in many diseases of the blood, bone, liver and intestinal tract. There are numerous examples of areas in protein hormone research which, if stimulated and strengthened by direct, concerted efforts, would yield valuable results directly applicable to diagnosis and patient care in addition to filling gaps in fundamental and clinical endocrine research. At present, pending future expansion, the Institute's hormone developmental research program is comprised of four contracts.

National Pituitary Agency: The Institute has contracted for the operation of the National Pituitary Agency (NPA) to increase and improve the collection of human pituitary glands and to provide for the distribution of purified human growth hormone (HGH) to qualified research scientists with the aid of a well-qualified advisory board of outside consultants. The NPA contract provides for the collection of human pituitary glands, fractionation of their major hormones, and distribution of HGH and other pure fractions to selected investigators for research purposes. At present, HGH can only be administered to patients in conjunction with clinical research studies because it is impossible to collect enough human pituitary glands to obtain sufficient HGH for treatment for all of the children suffering from hypopituitary dwarfism in the United States.

Other Efforts: Another contract provides access for American investigators to the Steroid Reference Collection of the British Medical Research Council. This collection, which includes literally hundreds of reference samples of steroids of highest purity, is the only resource of this kind in the world. Investigators in the United States, including grantees of the Institute, require access to such a collection to facilitate and expedite their research since there is no counterpart in the United States to many of these standards.

Another project in this program provides for the collection of rat pituitary glands on a large scale and for their extraction and fractionation to yield purified standardized pituitary hormones; growth hormone, lactogenic hormone, follicle stimulating hormone, and luteinizing hormone. These purified hormones are being made available to qualified, interested investigators with the aid of a specially constituted group of outside scientific consultants. This project which had been strongly endorsed by investigators in endocrinology provides a much needed source of purified rat pituitary hormones for bioassay chemical studies and laboratory studies which have been held back to date for lack of the purified hormone fractions.

The fourth contract in this program is aimed at providing, in reasonably large quantities, the biologically active metabolite of conventional vitamin D, "1,25 DHCC" (a product of internal conversion by the liver and kidneys of vitamin D), to a large number of investigators who are waiting to use it in crucial experiments on calcium and bone metabolism. The substance has only recently been isolated and identified and is not yet available through any other source.

Metabolism and Other Metabolic Diseases

The Institute supports basic and clinical research on all the complex chemical changes which take place in body tissues, and on the cellular level, which represent the biochemical basis for all life processes from minute-to-minute energy conversion through growth and aging. This includes studies of enzymes and their substrates, intermediary metabolites, and minerals, with particular emphasis on regulation of metabolism in normal and disease states. The Institute serves as the focus of research support related to specific metabolic diseases of genetic origin such as cystic fibrosis, phenylketonuria, Wilson's disease, galactosemia, the various glycogen storage diseases, congenital nonhemolytic jaundice, and many others.

Although diabetes and cystic fibrosis are the most widely known of the inherited metabolic diseases, literally hundreds of other such disorders afflict untold thousands of patients. Cystic fibrosis, a serious and complex disease of children and young adults, has an incidence of one in every 1,500 to 2,000 live births. As a cause of death in children under 15 years, it outranks many other better known diseases such as diabetes. Although cystic fibrosis has been recognized as a specific disease only since 1938, its increasing recognition throughout the world has identified it as a significant public health problem wherever the state of medicine is advanced enough so that the disease is recognized as such. In the United States, it is the source of significant human suffering and financial distress in families who have a child who is a victim of this, as yet uncontrollable, metabolic disease.

Recognition of hereditary metabolic diseases, as well as understanding of the mechanisms by which they produce injury and dysfunction, has increased greatly over the past half century. Further emphasis needs to be placed on early recognition of these inborn errors of metabolism inasmuch as improved medical management might delay the onset of complications and may even permit a long survival in some instances.

Many metabolic diseases are known to result from a deficiency of a single enzyme without which normal chemical reactions cannot take place in the body. Of the therapeutic approaches to diseases due to a hereditary enzyme deficiency, artificial induction of enzyme activity or provision of the missing enzyme from an outside source are in many ways the most attractive, and research in this area is expected to be supported during the next year.

Research is aimed at defining specifically all the biochemical aberrations and the consequent clinical manifestations associated with metabolic diseases. In the case of cystic fibrosis in particular, research presents difficult problems because the basic biochemical defect is not yet fully understood, and several organ systems are involved. Promising areas of research, especially the identification of the basic biochemical lesion and the development of new methods for diagnosis, treatment, and control are being pursued. Since the genetic character of cystic fibrosis makes the disorder especially pernicious, an important goal of the program is to develop a reliable, simple method of identifying carriers of the inherited trait so that families at risk can be identified and provided genetic counseling.

Objectives in 1974 and 1975

As a result of the release of 1973 unobligated balances in 1974, approximately 84 research grants and research and development contracts, 34 fellowships and career awards and 13 training grants will be awarded.

From the new budget authority available in 1974, it is estimated that 646 research grants and research and development contracts will be awarded. As a result of the termination and phase-out of current training programs, it is estimated that 137 previously committed continuation awards will be made under the fellowship, career development award and training grant programs. In addition, approximately 21 new or competing fellowships and career development awards will be funded for either a single year or for multiple years so as not to create a continuation cost in 1975. Under the new modified Research Training Program being initiated in 1974, 48 post-doctoral M.D.'s and Ph.D.'s will be trained for careers in research and/or teaching.

Also in 1974, a new regional research center grant program will be initiated. Although a modest beginning is anticipated in 1974, a significant program will be developed in 1975.

In recognition of the wide range of side effects from diabetes, a disease which affects the blood vessels, eyes, nervous system and kidneys, among other organ systems, an Inter-Institute Committee on Diabetes is being established to assure coordinated programs of research by the various Institutes. Other Institutes represented on the committee will include the national institutes of Heart and Lung, Eye, Neurological Diseases and Stroke, Child Health and Human Development, and General Medical Sciences.

Approximately 660 research grants and research and development contracts, will be awarded in 1975. The phase-out of the fellowship, career award and training grant program will be nearly completed and only 58 previously committed continuation awards will be made. The new modified Research Training Program which was initiated in 1974 will double in its second year and approximately 94 post-doctoral M.D.'s and Ph.D.'s will receive training for future careers in research or training.

Program plans for 1975 include expansion of the program for regional research centers for diabetes and related metabolic and endocrine disorders which was initiated in 1974 and approximately five centers will be supported in 1975. Increased use of the contract mechanism will also be made to further research and development efforts in the areas of synthesis of insulin, transplantation of insulin producing cells and to develop standard immunoassay resources for endocrine studies.

Digestive Diseases and Nutrition

Authorizing Legislation: Public Health Service Act Title IV Part D

	1974 Base *		1975		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits.........	---	---	---	---	---	---
Other expenses.........	---	$26,009,000	---	$26,650,000	---	+$641,000
Total.........	---	26,009,000	---	26,650,000	---	+641,000
Subactivities:						
Digestive Diseases...	---	18,186,000	---	18,087,000	---	-99,000
Nutrition............	---	7,823,000	---	8,563,000	---	+740,000
Total.........	---	26,009,000	---	26,650,000	---	+641,000
Budget Mechanism:						
Research Grants:						
Regular............	---	20,292,000	---	20,539,000	---	+247,000
Special............	---	853,000	---	2,641,000	---	+1,788,000
Subtotal.........	---	21,145,000	---	23,180,000	---	+2,035,000
Fellowships..........	---	546,000	---	600,000	---	+54,000
Training Grants......	---	2,208,000	---	360,000	---	-1,848,000
Research & Development Contracts..........	---	2,110,000	---	2,510,000	---	+400,000
Total.........	---	26,009,000	---	26,650,000	---	+641,000

* Excludes 1973 appropriation restorations.

Digestive Diseases

The digestive diseases program encompasses research of organ systems associated with the gastrointestinal tract, including salivary glands, esophagus, stomach, pancreas, liver, gallbladder, and small and large intestines. Research activity is concerned with the basic aspects of the anatomy, histology, physiology, endocrinology, and biochemistry of the gastrointestinal tract in health and their aberrations in different disease states. Efforts include studies of the cause, prevention, diagnosis and treatment of specific diseases such as esophagitis, peptic ulcer, pancreatitis, inflammatory bowel disease, malabsorption syndrome, gallstones, cirrhosis, hepatic coma, and many others.

Of all the causes of disability due to illness in our country, digestive diseases rank second. Over two million Americans are impaired in some degree by digestive diseases; of these, 1.2 million are limited in performing useful work, and 400,000 are totally disabled. Each year

Americans spend nearly 300 million man-days away from work and 116 million man-days in bed because of acute and chronic digestive diseases. In economic terms, the total cost of illness resulting from digestive disease is estimated at eight billion dollars per year or one percent of the gross national product.

Peptic ulcer will strike about 10% of all adults in the United States at some time during life. Some of the most exciting research in peptic ulcer today revolves around gastrin, the hormone which stimulates secretion of gastric acid (excessive secretion of the latter is believed to underlie the disorder). The laboratory synthesis of gastrin has provided an important research tool for the study of peptic ulcer, in which acid secretion is necessary for the occurrence of the disease process. In rats, the experimental induction of immune antibodies against gastrin can inhibit its potent gastric acid stimulatory action. Recently, novel types of antihistaminic drugs have been found which counteract gastric secretion. New approaches to suppression of gastric hypersecretion which leads to peptic ulcer merit support in Fiscal Year 1975.

The two major liver diseases, cirrhosis and hepatitis, are both crippling and potentially fatal diseases of great social and economic importance. A most rapidly moving field has been the finding of an association between the presence of a virus-like particle (Australia antigen) and a type of hepatitis transmitted primarily through blood transfusion or by contaminated hypodermic needles. There is some evidence that fatal liver necrosis or cirrhosis occurs only in those cases of acute viral hepatitis in which the Australia antigen is present. The reasons for chronic liver injury and subsequent cirrhosis in both alcoholic and viral liver injury are not fully established but are crucial to understanding and prevention of the diseases.

Among the many research studies which will continue to be supported during Fiscal Year 1975 are investigations into the possibility of dissolving gallstones to alleviate the need for recourse to surgery. Although medical scientists have been looking for methods to dissolve gallstones for many years, there have been no indications until recently that any medical treatment of gallstones might serve as an alternative to the surgery ultimately performed on one-half of the 800,000 new cases of symptomatic cholelithiasis which develop each year. Results published showed that long-term administration of a naturally occurring bile acid, chenodeoxycholic acid, led, in some patients, to dissolution of cholesterol gallstones which comprise 90 percent of the gallstones found in the United States. Based on the encouraging results of this research, plans have been formulated for clinical trials to determine the safety and efficacy of chenodeoxycholic acid treatment in dissolving cholesterol gallstones.

During this fiscal year, the Institute will make plans to support a number of Digestive Diseases and Nutrition Centers. Initially, the Digestive Diseases and Nutrition Programs of the NIAMDD will accept proposals for Centers devoted to investigations of obesity, peptic ulcer, hepatitis and cirrhosis. The scientific community will be informed when support is available for Centers involved with other areas of research. The objectives of the Centers are to establish environments to develop new, multidisciplinary research approaches to digestive and nutritional diseases, as well as to find ways to improve diagnosis, treatment, and prevention of these disorders.

As part of the Institute's efforts to intensify program efforts in the area of digestive diseases, the new collaborative research project, the National Cooperative Crohn's Disease Study, will continue in Fiscal Year 1975. This study is designed to examine the efficacy of several commonly used regimens in the treatment of regional ileitis (an inflammatory disease of the bowel known as Crohn's Disease), which has devastating effects on its patients, young adults in particular, causing prolonged periods of hospitalization and frequently leading to abdominal operations involving resection or removal of portions of the intestine.

The study, involving eight university medical centers, is a controlled, randomized clinical evaluation of the efficacy of three currently used drugs, prednisone, azulfidine and azathioprine, compared to a placebo, to determine the effectiveness of these agents. The study will initially examine each drug's effectiveness in preventing intensification of the disease, and the second phase will determine the effect of each drug in preventing recurrence of the disease.

The initiation and broadening of a contract effort by the NIAMDD to evaluate the efficacy and safety of chenodeoxycholic acid in dissolving cholesterol gallstones will also continue in the new year.

Nutrition

The Institute's nutrition program will continue to focus on those aspects of basic and clinical nutritional sciences which have particular relevance to improvement of human health and longevity. In the main, these are concerned with advancement of knowledge concerning the nutritional role of vitamins, trace minerals and elements, proteins and amino acids, fats, fatty acids and carbohydrates, and their relationships to normal and disordered states of metabolism. In certain of these areas, encouraging and important advances have been made during the past fiscal year by investigators whose research has been supported in large part by Institute funds.

Recent studies have demonstrated that the liver and then the kidney are the sites of conversion of vitamin D into the true or metabolically active form of the vitamin, essential for intestinal calcium transport and bone mineral mobilization. Subsequent research fully confirmed these findings and demonstrated a role of the kidney in regulation of plasma calcium through a typical "feed-back" mechanism. Chemical characterization of this "true" form of vitamin D is in progress, and its laboratory synthesis is being actively pursued. Its effectiveness in the treatment of renal osteodystrophy, vitamin D-resistant rickets, and related abnormalities of calcium metabolism will continue to be studied in Fiscal Year 1975.

In the meantime, research to facilitate prevention and control of obesity will continue to be supported by the Institute. Overweight and obesity to a degree that interferes with optimal health and longevity effects more than 20 per cent of adults in the United States, and constitutes a public health problem of major concern to the lay public and physicians. Attention will be given to morphogenesis of adipose tissue cells, multiple aspects of lipids and lipid metabolism, effects of fasting and periodicity of eating, neural and other factors influencing appetite, endocrine dysfunctions and hereditary factors.

Objectives in 1974 and 1975

As a result of the release of 1973 unobligated balances in 1974, approximately 43 research grants and research and development contracts, 20 fellowships and career awards and 9 training grants will be awarded.

From the new budget authority available in 1974, it is estimated that 338 research grants and research and development contracts will be awarded. As a result of the termination and phase-out of current training programs, it is estimated that 79 previously committed continuation awards will be made under the fellowship, career development award and training grant programs. In addition, approximately 19 new or competing fellowships and career development awards will be funded for either a single year or for multiple years so as not to create a continuation cost in 1975. Under the new modified Research Training Program being initiated in 1974, 24 post-doctoral M.D.'s and Ph.D.'s will be trained for careers in research and/or teaching.

Also in 1974, a new regional research center grant program will be initiated and developed into a significant program by 1975.

Approximately 343 research grants and research and development contracts, will be awarded in 1975. The phase-out of the fellowship, career award and training grant program will be nearly completed and only 34 previously committed continuation awards will be made. The new modified Research Training Program which was initiated in 1974 will double in its second year and approximately 47 post-doctoral M.D.'s and Ph.D.'s will receive training for future careers in research or training.

The major initiative in 1975 in this activity will be to develop the regional centers program to conduct research and clinical investigations in gastroenterology and nutrition aimed at better diagnosis and treatment and eventual prevention of the various disease entities in these areas.

Kidney Disease

Authorizing Legislation: Public Health Service Act Title IV Part D

	1974 Base *		1975		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits.........	---	---	---	---	---	---
Other expenses.........	---	$18,121,000	---	$17,335,000	---	-$786,000
Total.........	---	18,121,000	---	17,335,000	---	-786,000

	1974 Base *		1975		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Budget Mechanism:						
Research Grants:						
Regular.............	---	12,362,000	---	12,659,000	---	+297,000
Special.............	---	223,000	---	50,000	---	-173,000
Subtotal..........	---	12,585,000	---	12,709,000	---	+124,000
Fellowships..........	---	364,000	---	600,000	---	+236,000
Training Grants......	---	1,503,000	---	156,000	---	-1,347,000
Research & Development Contracts...........	---	3,669,000	---	3,870,000	---	+201,000
Total.........	---	18,121,000	---	17,335,000	---	-786,000

* Excludes 1973 appropriation restorations.

Nephrology in its broadest sense is defined as the study of the kidney and related organs in health and disease. The primary functions of the kidney include elimination of nitrogenous and other waste products as well as regulation of the body's water balance, and that of salts and minerals in the blood and tissues. In addition, the kidney is implicated in the regulation of blood pressure and in other hormonal activities, including stimulation of red blood cell formation.

In an attempt to improve the understanding of the kidney and related urinary tract organs, the Institute supports a broad program, which includes studies of the basic mechanisms of kidney function and the urinary tract in both health and disease. Some of the major kidney/urologic diseases include pyelonephritis, glomerulonephritis and other immunologic diseases of the kidney, the nephrotic syndrome, polycystic disease, urolithiasis (kidney stones), benign prostatic hypertrophy, urinary tract infections, renal hypertension, and end-stage kidney disease (uremia). The precise etiological bases of most of these diseases are still unknown but infections, genetic defects, hypertension and systemic blood vessel disease, aberrations of immune mechanisms, and chemical and mechanical injury are all considered to contribute.

Irreversible end-stage kidney disease or uremia is recognized from a composite of signs and symptoms caused by the kidney's inability to remove the body's metabolic wastes and to regulate its internal chemistry. Although two dramatic therapeutic approaches to end-stage kidney disease, namely chronic hemodialysis and kidney transplantation, have been developed to cope with fatal end-stage kidney disease, current knowledge allows no primary prevention of chronic kidney disease with the exception of infections of the urinary tract, and except for those patients who are detected to have abnormalities of the collecting and excretory system which may be corrected surgically.

It is estimated that on a national basis the death rate from primary or secondary kidney disease is 29 per 100,000 population. The 60,000 annual deaths due to kidney failure are exceeded only by deaths due to heart disease, cancer, cerebral vascular accidents and traumatic accidents. Eight million individuals suffer from disorders of the kidney or urinary tract.

Although a wide range of investigations of the kidney have increased our ability to cope with the problem of kidney failure, research efforts in Fiscal Year 1975 will continue towards achieving prevention and control of immunologic glomerular kidney disease, hypertensive kidney disease, and chronic infections. In addition, studies will continue in the treatment of early kidney failure, which should reduce considerably the need for dialysis or transplantation. The new fiscal year will see continued research to evaluate the effectiveness of varied combinations and doses of drugs used to prevent the rejection of grafted kidneys, the main problem in transplantation.

Graft rejection occurs because the body's internal defense system attacks foreign tissues and organs just as it attacks invaders such as viruses and disease germs. Although tissue typing and subsequent rational matching of donor kidneys and transplant recipients has helped to alleviate this problem, physicians use immunosuppressive drugs as an additional control. These drugs are toxic, and tend to weaken the body's immunity to infectious microorganisms as well as to foreign tissues. Use of the drugs must be carefully regulated if the patient is to retain his transplant without suffering the possible adverse effects of a weakened immunological system.

One such promising investigation will study animals that have kidney transplants by treating them with various combinations and dosages of new and currently used immunosuppressive agents to determine which combination therapy best prevents transplant rejection with few, if any, side effects. The condition of each animal will be monitored, through weekly laboratory tests of its blood and urine and periodic renal biopsies, to evaluate the effects of the drugs on both the health of the animal and the viability of the transplant.

Artificial Kidney Program

The Artificial Kidney-Chronic Uremia Program was established in 1965 by Congress for ". . . development of a better artificial kidney than the machines which now exist." The goals of the Program are to provide scientific data and technology leading to improved patient care and lower maintenance costs for patients with irreversible chronic kidney failure. Thus the program endeavors to improve artificial kidney apparatus and methodologies, to increase their effectiveness, to decrease their initial and operational cost, and to improve rehabilitation of chronic dialysis patients. Development of new dialysis apparatus and methods is hampered by incomplete knowledge of the uremic syndrome. Hence research into the fundamental aspects of the toxic nature of uremia and basic and clinical studies of chronic dialysis are critical to attaining program goals, and are currently receiving increasing emphasis.

In the United States today, an estimated 60,000 individuals die each year as a result of irreversible kidney failure. The diseases which originally initiate the chain of events which terminates with advanced kidney failure vary considerably in nature. Regardless of origin, serious progressive kidney damage leads to fatal irreversible kidney failure. Annually, about 10,000 patients with end-stage kidney disease are medically suitable for long-term dialysis or transplant treatment. Transplant patients must also be maintained for a portion of the time by dialysis and may have to return to dialysis in case the grafted organ is rejected and ceases to function. Because of a shortage of available organs, transplantation, so far, has been available to only 20-25% of this patient population. Beginning on July 1, 1973, new legislation provided MEDICARE funds for all end-stage disease patients covered by Social Security, or their dependents, who require dialysis treatment or kidney transplantion. It is estimated that within a few years approximately 40,000 patients will be kept alive with maintenance dialysis at a cost of between $600 to $800 million. Any improvement in current dialysis therapy which can be developed by the Artificial Kidney-Chronic Uremia Program which would enhance the medical rehabilitation of the patients or would make the currently costly and lengthy treatment briefer and more effective, will bring about significant human benefits in terms of well-being and ability to work full-time, and will result in savings of Federal funds.

In recent years, hemodialysis has become a predictable maintenance therapy. Through development support of this program, a new generation of "hollow fiber" dialyzers is now being produced commercially. One development initiated by this program is that of a semi-portable artificial kidney machine, capable of detoxification of the uremic patient without being connected to a water supply or drain. Significant improvements have been made in the efficiency of flat-plate dialyzers, markedly decreasing the required dialysis time. A recent development is a new concept which involves use of a single (rather than double) needle for access to the bloodstream, an approach meeting with high patient acceptance. Peritoneal dialysis has been brought to the stage of an acceptable alternative to hemodialysis, by development of an indwelling silicone rubber catheter which permits repeated, safe access to the peritoneal cavity, and an automated dialysate supply system.

The dialysis membrane is the heart of the artificial kidney system, and a number of new types developed by the program will be undergoing clinical trials in the coming fiscal year.

Since its origin, the program has supported investigations of the pathophysiology of uremia. Considerable research effort on abnormal metabolites of uremia has not yet achieved a level of full understanding of this complex array of abnormalities. Significant progress, however, has occurred in the understanding of uremic bone disease, now permitting control of this complication of dialysis. Studies will continue to be devoted to the mechanisms of uremic anemia, neurological malfunctions, and other complications of uremia such as hyperlipidemia.

One of the most important activities underway is the quantitation of dialysis therapy now under study using different experimental membranes or altered dialysis protocols, with the objective of defining quantitatively the level of clearance necessary for each solute molecular weight range to hold various clinical parameters to near-normal values. Such research is now possible because of the availability of a wide range of membranes, dialysis protocols, and new, rational research hypotheses.

Continued support of membrane-related research to develop lower cost coil dialyzers and improved hollow fiber devices and documentation of dialyzer performance with reuse is planned. The area of greatest emphasis will be on improved therapy and its evaluation to provide meaningful quantitative guidelines for definition of adequate dialysis treatment.

Objectives in 1974 and 1975

As a result of the release of 1973 unobligated balances in 1974, approximately 25 research grants and research and development contracts, 4 fellowships and career awards and 6 training grants will be awarded.

From the new budget authority available in 1974, it is estimated that 256 research grants and research and development contracts will be awarded. As a result of the termination and phase-out of current training programs, it is estimated that 30 previously committed continuation awards will be made under the fellowship, career development award and training grant programs. In addition, approximately 7 new or competing fellowships and career development awards will be funded for either a single year or for multiple years so as not to create a continuation cost in 1975. Under the new modified Research Training Program being initiated in 1974, 24 post-doctoral M.D.'s and Ph.D.'s will be trained for careers in research and/or teaching.

Approximately 259 research grants and research and development contracts, will be awarded in 1975. The phase-out of the fellowship, career award and training grant program will be nearly completed and only 6 previously committed continuation awards will be made. The new modified Research Training Program which was initiated in 1974 will double in its second year and approximately 47 post-doctoral M.D.'s and Ph.D.'s will receive training for future careers in research or training.

In 1975 a new research and development contract program will be initiated in the area of urologic and kidney diseases. The new program will be distinct from the Artificial Kidney Program which is targeted toward less costly, more effective hemodialysis treatment, and will be aimed at prevention and diagnosis and treatment of diseases of the kidneys and urologic tract.

Hematology

Authorizing Legislation: Public Health Service Act Title IV Part D

	1974 Base *		1975		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits.........	---	---	---	---	---	---
Other expenses.........	---	$11,039,000	---	$10,518,000	---	-$521,000
Total.........	---	11,039,000	---	10,518,000	---	-521,000

Budget Mechanism:

	1974 Base *		1975		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Research Grants:						
Regular.............	---	8,619,000	---	9,289,000	---	+670,000
Special.............	---	321,000	---	273,000	---	-48,000
Subtotal..........	---	8,940,000	---	9,562,000	---	+622,000
Fellowships..........	---	393,000	---	600,000	---	+207,000
Training Grants......	---	1,606,000	---	206,000	---	-1,400,000
Research & Development Contracts...........	---	100,000	---	150,000	---	+50,000
Total.........	---	11,039,000	---	10,518,000	---	-521,000

* Excludes 1973 appropriation restorations.

Institute support for hematology in Fiscal Year 1975 will cover a wide range of studies which may be characterized as either working towards control of blood disease or utilizing blood as a biological tool to study other biomedical problems. In the comprehensive field of hematology, which is dealt with by several Institutes at the National Institutes of Health, a number of specific areas are identified as targets for the extramural research program of the NIAMDD. These are: genetic disorders of hemoglobin and its production such as Cooley's anemia and other thalassemias; the non-genetic anemias and disorders of blood cell production; enzymatic and metabolic defects of blood cells; and immunology of organ transplantation and of autoimmune hematologic disease. The hypochromic anemias, a broad category of blood disorders characterized by deficient red cell production, also constitutes a wide health problem, including, as it does, iron deficiency anemia and certain vitamin deficiency anemias.

Although hematologic diseases, with the exception of leukemia, are not among the leading causes of death, the well being and quality of life for many persons are significantly diminished by them. For example, up to 40% of the patients seen by hematologists are suffering from anemia. In addition, the course and prognosis for other diseases can be seriously affected by attendant hematologic problems such as the chronic anemia secondary to chronic kidney disease, malignancy and gastrointestinal and endocrine disorders. Recent nutrition surveys have uncovered a larger-than-expected extent of mild to moderate iron deficiency anemia in our population, particularly among infants, female teenagers, and women of childbearing age. Studies with objectives related to the absorption and utilization of different types of iron compounds will be pursued during the next fiscal year.

While there is a steady growth of knowledge about the blood diseases, further basic research is needed to understand better the various relevant disease processes and to permit development of effective therapy. Knowledge of the molecular defect in sickle cell anemia is opening up possibilities for chemical amelioration of the symptoms of the defect, and now micro-techniques can detect the abnormal hemoglobin in first trimester fetuses. Recent advances in the isolation and purification of certain blood fractions essential for the normal clotting process ("Factor VIII") now make possible effective stoppage of bleeding in patients with hemophilia and even permit major surgery after prophylactic administration of purified antihemophilic factor.

The often fatal end-result of repeated blood transfusion, the only known therapy for Cooley's anemia victims, is the accumulation of iron deposits in vital organs. Development of a safe, effective oral chelating agent, to remove excess iron resulting from frequent blood transfusions essential for maintenance therapy in this disease, would end the major objection to transfusion therapy, which is otherwise generally well-tolerated. Chemists now consider that such an agent could be developed with present technology, and this pursuit will remain a goal of Institute-supported researchers in the next fiscal year.

Objectives in 1974 and 1975

As a result of the release of 1973 unobligated balances in 1974, approximately 18 research grants and research and development contracts, 7 fellowships and career awards and 6 training grants will be awarded.

From the new budget authority available in 1974, it is estimated that 141 research grants and research and development contracts will be awarded. As a result of the termination and phase-out of current training programs, it is estimated that 38 previously committed continuation awards will be made under the fellowship, career development award and training grant programs. In addition, approximately 9 new or competing fellowships and career development awards will be funded for either a single year or for multiple years so as not to create a continuation cost in 1975. Under the new modified Research Training Program being initiated in 1974, 24 post-doctoral M.D.'s and Ph.D.'s will be trained for careers in research and/or teaching.

A small but vitally important contract program will be initiated to develop a chelating agent to prevent or reduce the build-up of excess iron which is the most immediate cause of death of victims of Cooley's Anemia. As the "lead" Institute in this area, the NIAMDD will continue to coordinate the augmenting and complementing activities of other organizations of the NIH, including the National Heart and Lung Institute, National Institute of General Medical Sciences, National Institute of Child Health and Human Development and the Division of Research Resources.

Approximately 149 research grants and research and development contracts, will be awarded in 1975. The phase-out of the fellowship, career award and training grant program will be nearly completed and only 16 previously committed continuation awards will be made. The new modified Research Training Program which was initiated in 1974 will double in its second year and approximately 47 post-doctoral M.D.'s and Ph.D.'s will receive training for future careers in research or training. New initiatives in Cooley's Anemia will be explored.

Intramural Laboratory and Clinical Research

Authorizing Legislation: Public Health Service Act Title IV Part D

	1974 Base *		1975 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits.........	451	$10,304,000	451	$10,256,000	---	-$48,000
Other expenses.........	---	12,180,000	---	13,057,000	---	+877,000
Total.........	451	22,484,000	451	23,313,000	---	+829,000

* Excludes 1973 appropriation restorations.

Introduction

The mission of the intramural research area of the Institute is to obtain information and knowledge for the understanding of the fundamental biological processes underlying the major diseases within the Institute's purview. Over 260 research projects including various combinations of laboratory, clinical, epidemiological and biometric investigations are conducted in facilities in Bethesda, Maryland and Phoenix, Arizona. Medical, biological, physical and chemical investigations range from studies of fundamental mechanisms, to specific disease oriented laboratory research, to clinical evaluation and treatment programs. Close collaboration with scientists of other NIH institutes, other government agencies and outside investigators ensure a minimum of duplication and a maximum exchange of research findings.

Arthritis and Rheumatism

Like their colleagues in a number of laboratories and clinics, Institute investigators in Bethesda are studying the possibility that rheumatoid arthritis is the result of chronic inflammation, probably triggered by an abnormal immune reaction. Although the mechanisms of damage remain unproven and obscured, Institute researchers are endeavoring to discover whether the degenerative process results from an infection, an autoimmune reaction (mistaken attack by body defense systems on its own tissue), or a combination of these.

Mycoplasma from swine with experimentally induced arthritis will be examined further to determine how this infectious agent may induce pathological changes in joint tissues. In the treatment of rheumatoid arthritis, this coming year intramural investigators will continue to scrutinize closely an anti-cancer agent, cyclophosphamide. Although preliminary results have been promising, scientists are anxious to learn more about the mechanism of action of the drug and how to deal with its potent side effects which may place limitations on its more widespread use.

The relatively gradual destruction of cartilage, bone, and periarticular supporting structures, which is characteristic of rheumatoid arthritis and is its most disabling feature, is ascribed to invasion of the structures by chronic inflammatory granulation tissue (pannus). There is some reason to believe that timely surgical removal of this tissue will prevent progressive destruction, and thus research will include experimental synovectomies to ascertain their worth.

Like rheumatoid arthritis, systemic lupus erythematosus (SLE) is another connective tissue disorder. It develops in about 50,000 new patients each year, most often affecting people in the 20-40 year age group, particularly young women. Connective tissue, comprised mainly of collagen fibers and a glue-like basic matrix called "ground substance," makes up a large part of the body's tissues and is essential to its structure and function. SLE is manifested by various disorders in the structure and activity of the skin, joints, blood vessels and internal organs. It is an insidious, inflammatory disease of considerable gravity.

Although the cause of SLE is not known, much evidence points, as in the case of rheumatoid arthritis, to a disorder of the body's immune mechanism which may or may not be tied to a previous infectious process. The disease can appear as a result of hypersensitivity to certain drugs, and this phenomenon is among those being studied by Institute researchers at the NIH Clinical Center. Patients also are under investigation there in a study involving the immunosuppressive drugs cyclophosphamide and azathioprine in the treatment of certain of the complications of SLE.

Diabetes and Other Metabolic Diseases

A primary goal in Institute diabetes research is to understand the basic impairment of insulin activity, a complete knowledge of which would uncover some of the riddles now surrounding diabetes. Studies during the forthcoming year will center on the physiology of insulin, and how this hormone exerts its influence on cell membranes and cellular metabolism. Institute scientists will study ways in which insulin acts upon individual body cells primarily by binding to specific receptor sites on cell membranes. Scientists will also examine how the multiple effects of insulin, e.g., increased glucose transport into the cell, decreased mobilization of fat, increased glycogen synthesis, depend upon one or more "second messengers" that act within the cell, such as spermine and spermidine (which have been found to mimic intracellularly some of the actions of insulin) or "cyclic AMP." Continuance of such fundamental studies is essential for elucidation of the mechanisms by which insulin exerts its multifarious effects on cellular processes, and may permit development of rational and effective treatments for diabetic patients. Institute researchers will also continue clinical studies of cystic fibrosis, with additional basic studies in such disciplines as biochemistry, genetics, and molecular biology. Efforts will be geared toward uncovering the specific basic biochemical aberrations of this disease in expectation that in this way, improved detection, control and therapy will result. For example, since the components of external secretions play such important roles in the pathogenesis of cystic fibrosis, intensive studies will be conducted to isolate the abnormal factors in such exocrine gland secretions as saliva.

The Southwestern Field Studies Section will continue its epidemiological investigation of diabetes mellitus among Indians of the Southwestern United States, and in particular, the Pima Indians of Arizona. Various factors, including hereditary, environmental, dietary, and anthropological aspects that may have a bearing on the frequency and severity of these diseases are and will continue to be investigated. Selected findings are being contrasted with similar studies performed on other populations with different characteristics and environments.

The vascular complications of diabetes mellitus are responsible for the majority of the morbidity and mortality associated with diabetes mellitus. The relationship of hypertension to retinopathy in the diabetic appears to represent an important factor in the pathogenesis of the retinal changes, and one whose effect is potentially amenable to alteration by safe medical means, which will be evaluated in the coming year.

Endocrinology

One main thrust of Institute endocrinology research is to learn the precise mechanisms by which hormones influence the metabolism and physiology of man. Recent findings are leading to a better understanding of disorders of the parathyroid gland, such as hyperparathyroidism. This disease, marked by an oversecretion of the parathyroid hormone, causes decalcification of bone, an abnormally high blood calcium level, and can lead to kidney stones, bone cysts, and other problems.

In more clinically-directed research, Institute scientists will pursue their preliminary findings regarding the administration of thyroxine. The scientists have shown that weekly (rather than more frequent) administration of thyroxine, a synthetic thyroid hormone, is a safe and effective means of controlling hypothyroidism in young patients without cardiovascular disease.

Also, lithium has been shown to be effective in the treatment of hyperthyroidism. Its exact place in treatment will be evaluated in the coming year. The recent development of a highly sensitive radioimmunoassay for parathyroid hormone is expected to improve diagnostic accuracy for hypo- or hyper-parathyroid states and to allow measurement of rates of secretion of the hormone. Patients with hypercalcemia, hypophosphatemia, nephrocalcinosis, nephrolithiasis, or other manifestations of hyperparathyroidism are being studied.

Studies will be carried out on effects of calcium or EDTA infusions and changes in diet on the secretion of parathyroid hormone. Recent use of selective venous catheterization combined with radioimmunoassay for parathyroid hormone has proved a value also in localizing parathyroid tumors incompletely removed at earlier surgical explorations.

Attention will also be given to renal and gastrointestinal responses to the effects of the hormone. These studies will further be applied to selected patients with hypoparathyroidism, rickets, osteomalacia, vitamin D-resistant rickets, osteoporosis, and certain other abnormalities of bone metabolism.

A recent finding indicates that parathyroid function is an important influence on urinary excretion of cyclic 3'5'-AMP and that this nucleotide is involved in the mechanism of action of the parathyroid hormone. Clinical investigations based on these findings suggest that a constitutional defect of the hormonally sensitive enzyme adenyl cyclase may be the cause of pseudo-hypoparathyroidism, and further cases of this disorder will be studied.

In the meantime, Institute scientists will continue their study of amyloid, the waxy protein deposits accumulating in human organs such as the liver and kidney in the puzzling disease called amyloidosis. Institute research already has suggested that amyloid protein is derived from a fragment of an antibody molecule, the substance formed by the body's response to foreign infectious agents, and further study of this protein should lead to a clearer picture of the role of enhanced and prolonged antibody formation in the production of amyloid.

Amyloidosis is a serious disorder commonly associated with rheumatoid arthritis and tuberculosis, and other chronic infectious or inflammatory diseases, as well as with the normal aging process. No successful treatment is available as yet for amyloidosis, although cure of the underlying infection occasionally results in remission of this ultimately fatal disease. Perhaps illustrative of the Institute's research was an October 22, 1973 medical research article on the front page of the New York Times which stated: "Most of the little that is known about amyloidosis was learned in the last decade by Dr. George Glenner at the National Institutes of Health in Bethesda, Maryland." Dr. Glenner has been a pathologist with the National Institute of Arthritis, Metabolism, and Digestive Diseases since 1955.

Digestive Diseases

To emphasize further digestive disease research, the NIAMDD reorganized its intramural research activities on digestive disorders into a Digestive Disease Branch composed of four sections: Gastroenterology, Diseases of the Liver, Phoenix Clinical Research Section, and Physiology and Clinical Nutrition. The new Branch supersedes the former Digestive and Hereditary Diseases Branch, and will continue to conduct clinical and laboratory investigations to determine abnormalities in structure and function of the esophagus, stomach, small and large intestines, pancreas and liver, and research on certain hereditary metabolic diseases. Work will be directed at an understanding of human disease and its treatment in terms of underlying derangements in the body's metabolism and physiology. Because of the importance of digestive diseases and because the digestive tract lends itself particularly well to the pursuit of this goal and permits a ready extension of animal studies to man, this organ system is a primary focus of the Institute's clinical activities. In addition, since the inborn errors of metabolism constitute a direct clinical reflection of a chemical derangement, and since the inborn errors frequently affect segments of the digestive system, the Institute is also engaged in studies of such disorders. The causes and manifestations of intestinal malabsorption are numerous and varied. In many instances such fundamental problems as the etiology, the nature of the pathological physiology, the optimal therapy and the importance of hereditary factors still require extensive investigation.

The cost of the 300,000 cholecystectomies (gallbladder removals) performed annually in the U.S. approaches one billion dollars. Fifteen million people in this country alone are estimated to have gallstones with about three times the incidence in females compared with males. An exciting new concept of treating cholesterol gallstones medically rather than surgically has shown considerable promise. The oral administration of a natural bile acid, chendeoxycholic acid, has resulted in the diminution or disappearance of cholesterol gallstones in most of the subjects tested. The Digestive Diseases Branch will participate during this coming year in therapeutic trials of this medical approach to the dissolution of gallstones.

The Southwestern Field Studies Section had previously revealed that the Pima Indians of Arizona have a rate of gallbladder disease that is six times higher than that found in a similar study of Caucasians in Framingham, Mass. It has also been found that among the Pima Indians, gallbladder disease is extraordinarily frequent in both males and females, and that less than one half of the affected subjects had been recognized clinically.

The establishment of the patho-physiolcgic basis of cholesterol gallstone formation in the American Indian and other populations as the result of diminished bile salt secretion has led to the realization that the prevention and dissolution of gallstones by the oral administration of bile salts may be possible. The suitability of the Pima Indian population for the demonstration of the potential of this mode of therapy has led to the design of a clinical trial to determine the ability of cholic and chenodeoxycholic acid to dissolve asymptomatic gallstones. This trial will be implemented as soon as possible.

Hematology

Hematology represents an important part of the Institute's research mission. Among Institute research goals is a definition of the specific defects in various blood disorders, as well as knowledge of the precise steps in normal and abnormal blood clotting mechanisms, with application of resulting findings to improved diagnosis and therapy.

Institute clinical research in blood disease this coming fiscal year will stress, among other studies, the biochemistry of blood coagulation with particular reference to the development of better forms of therapy for various congenital and acquired hemorrhagic diseases. Such disorders as hemophilia A or B, von Willebrand's disease, hemophiloid conditions such as Factor V or Factor VII deficiency, circulating anticoagulants, afibrinogenemia, fibrinolysis, as well as obscure, undiagnosed bleeding disorders, will be studied. New approaches to therapy of acute and chronic idiopathic thrombocytopenic purpura (ITP) and thrombocytopenia of lupus will also be evaluated.

Objectives in 1975

The increase in this activity in 1975 is required for mandatory items primarily including annualization of the cost of recent pay increases and an increase of this Institute's proportionate share of increased costs of centrally furnished services such as patient care, computer services, maintenance of buildings and grounds, custodial services, communications, and transportation.

Research Management and Program Services

Authorizing Legislation: Public Health Service Act Title IV Part D

	1974 Base *		1975 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits.........	106	$2,227,000	106	$2,302,000	---	+$75,000
Other expenses.........	---	3,529,000	---	3,606,000	---	+77,000
Total.........	106	5,756,000	106	5,908,000	---	+152,000

* Excludes 1973 appropriation restorations.

Within this activity, general direction, coordination and administration of the resources of the total Institute are provided by the Institute Director, his immediate staff and the office of administrative management including contract negotiations and awards. The review and approval of grants functions include review for scientific merit and program relevance and maintenance of surveillance over each grant project. Scientific information functions are also conducted under this activity.

Nearly two-thirds of the resources of this activity are devoted to review and approval of grants functions including professional and supporting personnel who are responsible for the administration of the Institute's several grants activities. They assist in the planning and development of programs in research, training, and fellowships that will best serve to accomplish the desired results in the areas of disease interest for which this Institute is responsible; review and evaluation of research and training grant applications for presentation to the National Advisory Arthritis Council; required Council staff assistance; liaison with applicants, grantees, other components of NIH and the Department, advisory bodies, and interested organizations; continuous surveillance of scientific activities and progress; and recording and reporting of fiscal and scientific information relevant to all transactions.

In response to legislation which added "Digestive Diseases" and mandated certain organizational changes, an Associate Director for Digestive Diseases was appointed and that part of the departmentally approved reorganization of the extramural programs area was implemented. An unusual number of legislative proposals in the areas of diabetes, arthritis, kidney disease, and protection of human subjects require extensive staff participation.

In recognition of the wide range of side effects from diabetes, a disease which affects the blood vessels, eyes, nervous system and kidneys, among other organ systems, an Inter-Institute Committee on Diabetes is being established to assure coordinated programs of research by the various Institutes. Other Institutes represented on the committee will include the national institutes of Heart and Lung, Eye, Neurological Diseases and Stroke, Child Health and Human Development, and General Medical Sciences.

The entire increase in this activity is required for mandatory items primarily including annualization of the cost of recent pay increases and an increase of this Institute's proportionate share of increased costs of centrally furnished services such as patient care, receipt and initial review of all grant applications, computer services, maintenance of buildings and grounds, custodial services, communications, and transportation.

National Institute of Arthritis, Metabolism, and Digestive Diseases

Program Purpose and Accomplishments

Activity: Arthritis, Bone and Skin Diseases (Public Health Service Act Title IV Part D)

1974			1975 Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
---	$23,530,000	Indefinite	---	$22,379,000

Purpose: The National Institute of Arthritis, Metabolism, and Digestive Diseases (NIAMDD) conducts, fosters and assists research and training directed toward preventing, diagnosing, treating and controlling the numerous diseases encompassed in this activity. Programs are carried out through the use of research grants (approximately 80 to 85% of the funding), research and development contracts, fellowships and training grants.

Accomplishments and Objectives 1973/1974: In 1973, the programs in this activity awarded 329 research grants, 23 fellowships, 18 career development awards, 57 training grants and 2 research and development contracts.

As a result of the release of 1973 unobligated balances in 1974, approximately 40 research grants and research and development contracts, 10 fellowships and career awards and 12 training grants will be awarded.

From the new budget authority available in 1974, it is estimated that 330 research grants and research and development contracts will be awarded. As a result of the termination and phase-out of current training programs, it is estimated that 64 previously committed continuation awards will be made under the fellowship, career development award and training grant programs. In addition, approximately 10 new or competing fellowships and career development awards will be funded for either a single year or for multiple years so as not to create a continuation cost in 1975. Under the new modified Research Training Program being initiated in 1974, 33 post-doctoral M.D.'s and Ph.D.'s will be trained for careers in research and/or teaching.

Objectives, 1975: Approximately 346 research grants and research and development contracts, will be awarded in 1975. The new modified Research Training Program which was initiated in 1974 will double in its second year and approximately 66 post-doctoral M.D.'s and Ph.D.'s will receive training for future careers in research or training.

A modest increase in research and development contracts will be used to provide the emphasis for this activity in 1975. Specific program plans relate to the development of new biomaterials for surgically implantable artificial joints and to the new US-USSR cooperative program in arthritis.

NATIONAL INSTITUTES OF HEALTH

National Institute of Arthritis, Metabolism, and Digestive Diseases

Program Purpose and Accomplishments

Activity: Diabetes, Endocrinology and Metabolism (Public Health Service Act Title IV Part D)

1974			1975 Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
---	$46,197,000	Indefinite	---	$46,858,000

Purpose: The National Institute of Arthritis, Metabolism, and Digestive Diseases (NIAMDD) conducts, fosters and assists research and training directed toward preventing, diagnosing, treating and controlling the numerous diseases encompassed in this activity. Programs are carried out through the use of research grants (approximately 80 to 85% of the funding), research and development contracts, fellowships and training grants.

Accomplishments and Objectives 1973/1974: In 1973, the programs in this activity awarded 661 research grants, 63 fellowships, 64 career development awards, 68 training grants and 8 research and development contracts.

It is estimated that in 1974, 646 research grants and research and development contracts will be awarded. As a result of the termination and phase-out of current training programs, it is estimated that 137 previously committed continuation awards will be made under the fellowship, career development award and training grant programs. In addition, approximately 21 new or competing fellowships and career development awards will be funded for either a single year or for multiple years so as not to create a continuation cost in 1975. Under the new modified Research Training Program being initiated in 1974, 48 post-doctoral M.D.'s and Ph.D.'s will be trained for careers in research and/or teaching.

Also in 1974, a new regional research center grant program will be initiated. Although a modest beginning is anticipated in 1974, a significant program will be developed in 1975.

In recognition of the wide range of side effects from diabetes, a disease which affects the blood vessels, eyes, nervous system and kidneys, among other organ systems, an Inter-Institute Committee on Diabetes is being established to assure coordinated programs of research by the various Institutes. Other Institutes represented on the committee will include the National Institutes of Heart and Lung, Eye, Neurological Diseases and Stroke, Child Health and Human Development, and General Medical Sciences.

Objectives, 1975: Approximately 660 research grants and research and development contracts, will be awarded in 1975. The new modified Research Training Program which was initiated in 1974 will double in its second year and approximately 94 post-doctoral M.D.'s and Ph.D.'s will receive training for future careers in research or training.

Program plans for 1975 include expansion of the program for regional research centers for diabetes and related metabolic and endocrine disorders which was initiated in 1974 and approximately five centers will be supported in 1975. Increased use of the contract mechanism will also be made to further research and development efforts in the areas of synthesis of insulin, transplantation of insulin producing cells and to develop standard immunoassay resources for endocrine studies.

NATIONAL INSTITUTES OF HEALTH

National Institute of Arthritis, Metabolism, and Digestive Diseases

Program Purpose and Accomplishments

Activity: Digestive Diseases and Nutrition (Public Health Service Act Title IV Part D)

1974			1975 Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
---	$26,009,000	Indefinite	---	$26,650,000

Purpose: The National Institute of Arthritis, Metabolism, and Digestive Diseases (NIAMDD) conducts, fosters and assists research and training directed toward preventing, diagnosing, treating and controlling the numerous diseases encompassed in this activity. Programs are carried out through the use of research grants (approximately 80 to 85% of the funding), research and development contracts, fellowships and training grants.

Accomplishments and Objectives 1973/1974: In 1973, the programs in this activity awarded 308 research grants, 15 fellowships, 51 career development awards, 46 training grants and 8 research and development contracts.

As a result of the release of 1973 unobligated balances in 1974, approximately 43 research grants and research and development contracts, 20 fellowships and career awards and 9 training grants will be awarded.

From the new budget authority available in 1974, it is estimated that 345 research grants and research and development contracts will be awarded. As a result of the termination and phase-out of current training programs, it is estimated that 85 previously committed continuation awards will be made under the fellowship, career development award and training grant programs. In addition, approximately 16 new or competing fellowships and career development awards will be funded for either a single year or for multiple years so as not to create a continuation cost in 1975. Under the new modified Research Training Program being initiated in 1974, 20 post-doctoral M.D.'s and Ph.D.'s will be trained for careers in research and/or teaching.

Also in 1974, a new regional research center grant program will be initiated and developed into a significant program by 1975.

Objectives, 1975: Approximately 359 research grants and research and development contracts, will be awarded in 1975. The new modified Research Training Program which was initiated in 1974 will double in its second year and approximately 40 post-doctoral M.D.'s and Ph.D.'s will receive training for future careers in research or training.

The major initiative in 1975 in this activity will be to develop the regional centers program to conduct research and clinical investigations in gastroenterology and nutrition aimed at better diagnosis and treatment and eventual prevention of the various disease entities in these areas.

NATIONAL INSTITUTES OF HEALTH

National Institute of Arthritis, Metabolism, and Digestive Diseases

Program Purpose and Accomplishments

Activity: Kidney Disease (Public Health Service Act Title IV Part D)

1974			1975 Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
---	$18,121,000	Indefinite	---	$17,335,000

Purpose: The National Institute of Arthritis, Metabolism, and Digestive Diseases (NIAMDD) conducts, fosters and assists research and training directed toward preventing, diagnosing, treating and controlling the numerous diseases encompassed in this activity. Programs are carried out through the use of research grants (approximately 80 to 85% of the funding), research and development contracts, fellowships and training grants.

Accomplishments and Objectives 1973/1974: In 1973, the programs in this activity awarded 198 research grants, 16 fellowships, 5 career development awards, 31 training grants and 68 research and development contracts.

As a result of the release of 1973 unobligated balances in 1974, approximately 25 research grants and research and development contracts, 4 fellowships and career awards and 6 training grants will be awarded.

From the new budget authority available in 1974, it is estimated that 263 research grants and research and development contracts will be awarded. As a result of the termination and phase-out of current training programs, it is estimated that 31 previously committed continuation awards will be made under the fellowship, career development award and training grant programs. In addition, approximately 6 new or competing fellowships and career development awards will be funded for either a single year or for multiple years so as not to create a continuation cost in 1975. Under the new modified Research Training Program being initiated in 1974, 20 post-doctoral M.D.'s and Ph.D.'s will be trained for careers in research and/or teaching.

Objectives, 1975: Approximately 272 research grants and research and development contracts, will be awarded in 1975. The new modified Research Training Program which was initiated in 1974 will double in its second year and approximately 40 post-doctoral M.D.'s and Ph.D.'s will receive training for future careers in research or training.

In 1975 a new research and development contract program will be initiated in the area of urologic and kidney diseases. The new program will be distinct from the Artificial Kidney Program which is targeted toward less costly, more effective hemodialysis treatment, and will be aimed at prevention and diagnosis and treatment of diseases of the kidneys and urologic tract.

NATIONAL INSTITUTES OF HEALTH

National Institute of Arthritis, Metabolism, and Digestive Diseases

Program Purpose and Accomplishments

Activity: Hematology (Public Health Service Act Title IV Part D)

1974			1975 Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
---	$11,039,000	Indefinite	---	$10,518,000

Purpose: The National Institute of Arthritis, Metabolism, and Digestive Diseases (NIAMDD) conducts, fosters and assists research and training directed toward preventing, diagnosing, treating and controlling the numerous diseases encompassed in this activity. Programs are carried out through the use of research grants (approximately 80 to 85% of the funding), research and development contracts, fellowships and training grants.

Accomplishments and Objectives 1973/1974: In 1973, the programs in this activity awarded 151 research grants, 6 fellowships, 14 career development awards and 30 training grants.

As a result of the release of 1973 unobligated balances in 1974, approximately 18 research grants and research and development contracts, 7 fellowships and career awards and 6 training grants will be awarded.

From the new budget authority available in 1974, it is estimated that 150 research grants and research and development contracts will be awarded. As a result of the termination and phase-out of current training programs, it is estimated that 38 previously committed continuation awards will be made under the fellowship, career development award and training grant programs. In addition, approximately 8 new or competing fellowships and career development awards will be funded for either a single year or for multiple years so as not to create a continuation cost in 1975. Under the new modified Research Training Program being initiated in 1974, 20 post-doctoral M.D.'s and Ph.D.'s will be trained for careers in research and/or teaching.

A small but vitally important contract program will be initiated to develop a chelating agent to prevent or reduce the build-up of excess iron which is the most immediate cause of death of victims of Cooley's Anemia. As the "lead" Institute in this area, the NIAMDD will continue to coordinate the augmenting and complementing activities of other organizations of the NIH, including the National Heart and Lung Institute, National Institute of General Medical Sciences, National Institute of Child Health and Human Development and the Division of Research Resources.

Objectives, 1975: Approximately 159 research grants and research and development contracts, will be awarded in 1975. The new modified Research Training Program which was initiated in 1974 will double in its second year and approximately 40 post-doctoral M.D.'s and Ph.D.'s will receive training for future careers in research or training. New initiatives in Cooley's Anemia will be explored.

NATIONAL INSTITUTES OF HEALTH

National Institute of Arthritis, Metabolism, and Digestive Diseases

Program Purpose and Accomplishments

Activity: Intramural Laboratory and Clinical Research (Public Health Service Act Title IV Part D)

1974			1975 Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
451	$22,484,000	Indefinite	451	$23,313,000

Purpose: The mission of the intramural research area of the Institute is to obtain information and knowledge for the understanding of the fundamental biological processes underlying the major diseases within the Institute's purview. Over 260 research projects including various combinations of laboratory, clinical, epidemiological and biometric investigations are conducted in facilities in Bethesda, Maryland and Phoenix, Arizona. Medical, biological, physical and chemical investigations range from studies of fundamental mechanisms, to specific disease oriented laboratory research, to clinical evaluation and treatment programs. Close collaboration with scientists of other NIH institutes, other government agencies and outside investigators ensure a minimum of duplication and a maximum exchange of research findings.

Objectives, 1975: The increase in this activity in 1975 is required for mandatory items primarily including annualization of the cost of recent pay increases and an increase of this Institute's proportionate share of increased costs of centrally furnished services such as patient care, computer services, maintenance of buildings and grounds, custodial services, communications, and transportation.

NATIONAL INSTITUTES OF HEALTH

National Institute of Arthritis, Metabolism, and Digestive Diseases

Program Purpose and Accomplishments

Activity: Research Management and Program Services (Public Health Service Act Title IV Part D)

1974			1975 Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
106	$5,756,000	Indefinite	106	$5,908,000

Purpose: This activity provides the overall scientific and administrative management of the Institute. Functions include analysis evaluation, planning and direction of the various research and training programs; review, approval and administration of grants and contracts; collection and dissemination of scientific information; and administrative management of the operating areas of the Institute.

Accomplishments and Objectives 1973/1974: In 1973, in response to legislation which added "Digestive Diseases" and mandated certain organizational changes, an Associate Director for Digestive Diseases was appointed and that part of the departmentally approved reorganization of the extramural programs area was implemented. An unusual number of legislative proposals in the areas of diabetes, arthritis, kidney disease, and protection of human subjects required extensive staff participation. Use of data management systems was developed to meet growing workloads in the areas of personnel and contract management.

Objectives, 1975: The professional and supporting staff will continue to maintain close surveillance and overview required for the many existing programs of the Institute.

The increase in this activity is required for mandatory items primarily including annualization of the cost of recent pay increases and an increase of this Institute's proportionate share of increased costs of centrally furnished services such as patient care, receipt and initial review of all grant applications, computer services, maintenance of buildings and grounds, custodial services, communications, and transportation.

WEDNESDAY, MARCH 27, 1974.

NATIONAL INSTITUTE OF NEUROLOGICAL DISEASES AND STROKE

WITNESSES

DR. DONALD B. TOWER, ACTING DIRECTOR
DR. ROBERT S. STONE, DIRECTOR, NATIONAL INSTITUTES OF HEALTH
DR. DeWITT STETTEN, JR., DEPUTY DIRECTOR FOR SCIENCE, NATIONAL INSTITUTES OF HEALTH
DR. ELDON L. EAGLES, DEPUTY DIRECTOR, NATIONAL INSTITUTE OF NEUROLOGICAL DISEASES AND STROKE
ECKART WIPF, EXECUTIVE OFFICER, NATIONAL INSTITUTE OF NEUROLOGICAL DISEASES AND STROKE
ROBERT L. SITHENS, FINANCIAL MANAGEMENT OFFICER, NATIONAL INSTITUTE OF NEUROLOGICAL DISEASES AND STROKE
LEON M. SCHWARTZ, ASSOCIATE DIRECTOR FOR ADMINISTRATION, NATIONAL INSTITUTES OF HEALTH
LELAND B. MAY, ACTING DIRECTOR OF FINANCIAL MANAGEMENT, NATIONAL INSTITUTES OF HEALTH
CHARLES MILLER, DEPUTY ASSISTANT SECRETARY, BUDGET

Object Classification (in thousands of dollars)

Identification code 09-25-0886-0-1-651	1973 actual	1974 est.	1975 est.
Direct obligations:			
Personnel compensation:			
11.1 Permanent positions	8,057	8,753	9,175
11.3 Positions other than permanent	741	755	800
11.5 Other personnel compensation	167	185	195
Total personnel compensation	8,965	9,693	10,170
12.1 Personnel benefits: Civilian	942	1,020	1,059
21.0 Travel and transportation of persons	389	405	435
22.0 Transportation of things	68	70	93
23.0 Rent, communications, and utilities	480	481	531
24.0 Printing and reproduction	181	197	234
25.0 Other services	15,941	21,155	21,104
26.0 Supplies and materials	1,211	1,216	1,280
31.0 Equipment	590	615	679
41.0 Grants, subsidies, and contributions	78,601	108,320	84,373
Total direct obligations	107,368	143,172	119,958
Reimbursable obligations:			
21.0 Travel and transportation of persons	7	8	8
25.0 Other services	45	87	87
26.0 Supplies and materials	2	5	5
31.0 Equipment	56	100	100
Total reimbursable obligations	110	200	200
99.0 Total obligations	107,478	143,372	120,158

Personnel Summary

Total number of permanent positions	570	522	520
Full-time equivalent of other positions	40	37	37
Average paid employment	591	560	557
Average GS grade	8.5	8.6	8.6
Average GS salary	$14,260	$15,138	$15,473
Average salary of ungraded positions	$11,138	$12,018	$12,253

Program and Financing (in thousands of dollars)

	Identification code 09-25-0886-0-1-651	1973 actual	1974 est.	1975 est.
	Program by activities:			
	Direct program:			
	1. Communicative disorders	14,258	18,830	14,391
	2. Neurological disorders	52,091	65,372	55,425
	3. Stroke, nervous system, trauma	13,584	23,106	19,017
	4. Fundamental neurosciences	16,615	13,971	12,227
	5. Intramural laboratory and clinical research	6,624	7,684	8,233
	6. Research management and program services	9,094	14,209	10,665
	Total, direct program	112,266	143,172	119,958
	Reimbursable program:			
	5. Intramural laboratory and clinical research	110	200	200
	Total program costs, funded [1]	112,376	143,372	120,158
	Change in selected resources (undelivered orders)	−4,898		
10	Total obligations	107,478	143,372	120,158
	Financing:			
11	Receipts and reimbursements from: Federal funds	−110	−200	−200
25	Unobligated balance lapsing	23,269		
	Unobligated balance restored		−23,269	
	Budget authority	**130,694**	**119,903**	**119,958**
	Budget authority:			
40	Appropriation	130,672	125,000	119,958
	Withheld from obligation and expenditure (Public Law 93-192)		5,042	
41	Transferred to other accounts		−55	
42	Transferred from other accounts	22		
43	**Appropriation (adjusted)**	**130,694**	**119,903**	**119,958**
	Relation of obligations to outlays:			
71	Obligations incurred, net	107,368	143,172	119,958
72	Obligated balance, start of year	66,373	61,454	71,126
74	Obligated balance, end of year	−61,454	−71,126	−37,848
77	Adjustments in expired accounts	−1,532		
90	Outlays	110,755	133,500	153,236

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[1] Includes capital outlay as follows: 1973, $902 thousand; 1974, $615 thousand; 1975, $679 thousand.

NOTES

Excludes $2,123 thousand in 1974 and 1975 for activities transferred to (in thousands of dollars):

	1975
Research resources	2,009
Office of the Director	74
Departmental Management	40

Comparable amounts for 1973 ($2,123 thousand) are included above.

Excludes $63 thousand in 1975 for activities transferred to Assistant Secretary of Health: 1974, $63 thousand; 1975, $63 thousand.

Includes $152 thousand in 1975 for activities previously financed from the National Institute of General Medical Sciences: 1973, $152 thousand; 1974, $152 thousand.

Includes $22 thousand in 1974 and 1975 for activities previously financed from the Office of the Director. 1973, $22 thousand.

Excludes $55 thousand in 1974 and 1975 for activities transferred to Departmental Management. Comparable amount for 1973 ($55 thousand) is included above.

WITNESS INTRODUCTION

Mr. Flood. Now we have the National Institute of Neurological Diseases and Stroke. The presentation will be made by Dr. Donald B. Tower, the Acting Director.

We have a biographical sketch of you, Doctor, which we will place in the record at this point.

[The biographical sketch follows:]

Biographical Sketch

Name.—Donald Bayley Tower.

Position.—Acting Director, NINDS.

Birthplace and date.—Orange, N.J., December 11, 1919.

Education.—A.B., Harvard College, 1941; M.D., Harvard Medical School, 1944; M.Sc., McGill University, 1948; and Ph. D., McGill University, 1951.

Experience.—Acting Director, NINDS, May 1, 1973, to present; chief, Laboratory of Neurochemistry, IR, NINDS, May 1961 to May 1973; Head, Section on Amino Acid and Electrolyte Chemistry, LNC, IR, NINDS, May 1961 to present; Medical Director, USPHS (active), 1958 to present; Acting Associate Director, EP, NINDB, July 1967 to June 1968; Chief, Section on Clinical Neurochemistry, IR, NINDB, July 1953 to May 1961; Asst. Prof. of Experimental Neurology, McGill Univ., 1952–53; Associate Neurochemist, Montreal Neurological Institute, 1951–53; Externe (Neurology), National Hospital, Queen Square, London, 1951 (5 months); Research Fellow, Montreal Neurological Institute, 1947–51; Assistant Resident (Neurosurgery), Montreal Neurological Institute 1948–49; Medical officer, USNR, 1945–46 (active duty, Philippine theater); and Interne (surgery), University of Minnesota Hospitals, 1944-45.

Association membership.—American Academy of Neurology; American Association for the Advancement of Science; American Chemical Society; American Neurological Association; American Society for Neurochemistry (council member and treasurer); American Society of Biological Chemists; Canadian Neurological Society; Canadian Physiological Society; International Brain Research Organization (member, Central Committee); and International Society for Neurochemistry (council member).

Special awards, citations, or publications.—Alpha Omega Alpha; Sigma Xi; Markle Scholar 1951–53; Chief Editor (Western Hemisphere), Journal of Neurochemistry, 1968–73; Chairman, Neurochemistry Delegation to U.S.S.R. under U.S.-Soviet exchange program, 1969; Lennox guest lecturer, American Epilepsy Society, 1970; and author of over 90 scientific papers and monographs.

Mr. Flood. Do you have anybody you would like for us to know?

Dr. Tower. Dr. Eldon Eagles, Deputy Director of the Institute; Mr. Wipf, Executive Officer; and Mr. Sithens.

Mr. Flood. You have a prepared statement. How do you want to handle it?

Dr. Tower. I would like to read it.

GENERAL STATEMENT

Mr. Chairman and members of the committee. I am privileged to highlight for you the present status and anticipated progress of the research programs supported by the National Institute of Neurological Diseases and Stroke.

The Institute's mission is to promote and support research and research training in neurological and communicative disorders—disorders which afflict an estimated 20 percent of our population, from the youngest to the eldest of our citizens, at an annual cost of some $20 billion. Because most of the disorders are chronic, lifetime afflictions, they have a tragic impact on the quality of life. They can mean loss of personal independence and often an end to schooling, home-making, or wage earning. Hence the investment by the National Institute of Neurological Diseases and Stroke is focused on the problem areas that will provide an understanding of how nervous system functions are altered in disease and will lead to the development of effective preventive, diagnostic and therapeutic measures.

This year I want to summarize National Institute of Neurological Diseases and Stroke research support and progress in terms of four major budgetary program areas.

STROKE

The first major program area is stroke and nervous system trauma, representing 16.6 percent of our budget. In stroke research, we are currently devoting program funds to 16 clinical research centers, 11 stroke acute care research units, and eight stroke program projects as well as many individual research grants.

Stroke is the number three killer in our Nation, with an annual mortality of over 200,000 Americans. Of the 2.5 million survivors, 55 percent require special care and 15 percent remain bedfast for life. Thus, the clinical research centers and acute care research units represent invaluable resources for evaluation and application of promising research leads, especially in acute care and management.

NERVOUS SYSTEM TRAUMA

In nervous system trauma, we are funding four head injury clinical research centers, five acute spinal cord injury clinical research centers, and five spinal cord injury program projects. This year, we have set up a subcommittee of our National Advisory Council to examine the current status of central nervous system regeneration with special reference to spinal cord injuries, in order to identify promising research leads as well as areas where research needs to be stimulated. Like stroke, nervous system trauma is a major national problem since, of all accidents, injuries to the head and spinal cord constitute the No. 1 cripplers of America's young adults.

A common goal in stroke and nervous system trauma research is the protection of the brain or cord during the acute phase in order to preserve the viability and function of nerve cells. New noninvasive procedures have been developed to diagnose and monitor such problems. Of particular promise are new scanning instruments utilizing X-rays combined with computers to detect differences in nerve tissue density which reflect excess fluid (edema) and loss of blood supply (ischemia). The scanners are being applied to stroke and head injury problems in several centers. One is being purchased for the National Institute of Health Clinical Center with joint funds from National Institute of Neurological Diseases and Stroke, the National Cancer Institute and the Clinical Center.

With refinements in techniques of visualizing small blood vessels by X-ray, it is now known that after the commonest injury of brain or spinal cord—contusion or bruising—the most damaging factor is stoppage of local blood flow. The special significance of understanding the disturbances in the local regulation of blood supply and the consequent lack of tissue oxygen is the expectation of better drug therapy that will limit and minimize such local effects of stroke or trauma.

Major research efforts in preventive and rehabilitative prostheses also deserve mention.

HYPERTENSION

As you know, hypertension (high blood pressure) is the single most important precursor of heart attacks and strokes. The National Heart and Lung Institute supports a major campaign to combat hypertension. Through the National Institute of Neurological Diseases and Stroke-National Heart and Lung Institute Joint Council Subcommittee on Cerebrovascular Disease, efforts of the two institutes are coordinated. This year the National Institute of Neurological Diseases and Stroke embarked on a contract-supported major evaluation of "little stroke" attacks. This includes their recognition, natural history, and prognostic significance for subsequent major stroke, as well as effects of various preventive measures. For the long-term plight of a stroke or cord-injured victim, the National Institute of Neurological Diseases and Stroke is supporting an active intramural and contract program to develop various neural prostheses. Efforts to control bladder problems and to activate paralyzed limbs are now underway.

Altogether, I feel that these and other research advances supported by the NINDS stroke and nervous system trauma programs warrant a cautious note of optimism for more significant progress with these most frustrating problems.

COMMUNICATIVE DISORDERS

The second major program area supported by NINDS involves research in the communicative disorders—disorders of hearing, speech and language, and of other sensory systems, such as taste and smell, as well as the clinical problems that constitute the special province of the otolaryngologists. Current investment in these areas represent 13.5 percent of our budget. Even more than the current level of research is needed to deal with this vast array of problems. Research manpower is a major problem, and we are devoting special attention to promoting the training of researchers in the various relevant fields.

In addition, this year we established a new intramural Laboratory of Neurootology and have recruited an internationally recognized investigator as chief. To plan and oversee contract-supported research in communicative disorders, we have recruited an expert in speech and hearing as head of the section on communicative disorders in our collaborative and field research division. These major expansions, together with the expertise already available in our extramural grants division, now provide NINDS much of the research and managerial skills necessary to develop and monitor the additional research needed.

Rounding out our program in communicative disorders, we are devoting program funding to 2 clinical research centers, 3 outpatient research centers, and 18 program projects. In addition to general problems of deafness, specific projects give special attention to research on serous otitis media (a painless chronic middle ear affliction that is a major cause of hearing loss in children), on ototoxic agents (which damage the ear), on disturbances of the vestibular (balance) system, and on speech and language problems. Major NINDS intramural or contract-supported research encompasses several projects. These include: experimental utilization and evaluation of a recently developed master or hi-fi hearing aid; development of better speech analyzing aids or cues for the deaf; examination of the question of a critical age for language learning by children; evaluation of procedures and guidelines for speech therapy in aphasic adults; and studies of noise as it affects hearing and speech—a project (together with those of the National Institute of Environmental Health Sciences) included in the Federal effort on control of noise pollution coordinated by the Environmental Protection Agency. These NINDS programs reflect the uniqueness of communication as a human research problem.

NEUROLOGICAL DISORDERS

The third and largest program area encompasses research supported by NINDS in the neurological disorders other than stroke or central nervous system trauma. Some 47 percent of our budget is allocated to this program area.

In epilepsy, we are funding five clinical research centers, numerous individual research grants, and active intramural and contract projects. A major achievement this year has been the introduction of the new anticonvulsant drug carbamazepine (Tegretol), the first new drug for epilepsy to be approved in 14 years. NINDS scientists catalyzed this cooperative effort by the Food and Drug Administration (FDA), the pharmaceutical industry and the neurological community. We anticipate other new drugs may soon follow. A vital contribution of our intramural scientists has been the development and promotion of methods for determining the blood levels of anticonvulsant drugs so that rational, effective management of epileptic patients is now a reality.

The Institute is about to embark on the feasibility stage of a comprehensive epilepsy program. It is designed to coordinate one or more clinical research centers funded by NINDS with a comprehensive set of medical, social, rehabilitation, vocational, legal and education services designed to serve a large regional epileptic population and funded by other Federal, state and local groups. The concept derives from successful centers in several European countries and has stimulated much interest with the American neurological community.

In multiple sclerosis, a major event has been completion of the work by the National Advisory Commission on Multiple Sclerosis. The recommendations in the Commission's report submitted in February 1974 to the Secretary of HEW and to the Congress are under careful study. During this year NINDS is funding four clinical research centers and eight program projects. Current research into the cause of multiple sclerosis focuses on virological and immunological factors.

In neuromuscular disorders, NINDS is funding two clinical research centers and two program projects. Of special interest are: tissue culture studies of differentiating muscle cells aimed at elucidating the nature of intrinsic muscle disorders like muscular dystrophy; immunochemical studies utilizing antibodies against pure nerve-to-muscle receptor proteins—studies which provide animal models closely resembling human myasthenia gravis; the use by NINDS scientists of freeze-fracture electron microscopy to obtain a panoramic, birds-eye-view of cell membrane surfaces—a technique which has provided for the first time visualization of distinctive structural differences between nerve-to-nerve junctions that are excitatory and those that are inhibitory; and the fabrication of special electrodes that allow experimental recording of nerve and muscle electrical activity during free movement. This last achievement is a real breakthrough by NINDS scientists that permits the study of active muscles, in contrast to previous conventional techniques which are suitable only for muscles at rest.

NINDS scientists continue their progress in therapeutic approaches to the genetically determined lipid storage diseases. The enzymes previously shown to be missing in Gaucher's and Fabry's diseases have been purified from normal fresh human placenta and injected into afflicted patients achieving temporary reversal of the biochemical abnormalities in blood and liver. Purification of the enzyme missing in Niemann-Pick disease is well underway. For Tay-Sachs disease, both forms of the missing enzyme have been isolated and purified allowing us to formulate an explanation for the four variant or mutational forms of the disease.

NEUROSCIENCES

The fourth major program area covers research in the fundamental neurosciences, with current support representing 10.1 percent of the total NINDS budget. Many fundamental research projects cannot be readily identified with specific diseases, yet experience clearly shows the importance of providing significant support for such basic research. An example is the research on slow and latent viruses of the nervous system. This example represents one of the most significant and exciting developments in all of biology. NINDS scientists are in the forefront of these studies, which have revealed that the mammalian and human central nervous systems may harbor many varieties of virus species in latent or occult forms, including herpes, foamy, adeno, papova, myxo and paramyxo and various oncorna C-type viruses. Many of these viruses are experimentally tumorigenic. Whether any cause "spontaneous" brain tumors in man remains to be established. We must not overlook the possibility that the central nervous system may be a major source of viruses that can produce tumors elsewhere in the body. NINDS has just sponsored a workshop on the latest techniques for demonstrating the presence of latent virus species in host tissues. We are planning to use some of these new techniques to survey the dimensions of the potential problem posed by the harboring of such viruses in the brain.

Closely allied to the foregoing are significant new developments in immunology. We now know that many of the virally produced degenerative diseases of the central nervous system result from impaired cellular immunity, such as that seen in congentical rubella or SSPE (subacute sclerosing panencephalitis). In one the fetal immune system is not active so that the body does not recognize the virus as a foreign invader. In the other a blocking factor prevents access of the body's defenses to the viral invader. In still other cases defective viruses are produced in host cells and distort the usual host response to intact viruses. Many investigators think that multiple sclerosis may be a consequence of this last type of problem. When NINDS scientists infect monkey fetuses with one of several common viral species, hydrocephalus or spina bifida is regularly produced. Independently, two Institute scientists have evidence for X-ray activation of a latent virus within the host cell. Clearly immunological research of the most advanced type is essential to an understanding of the effects of viruses on nervous tissue. For this reason NINDS plans next year to augment its strong intramural virus research team by creating and staffing a Laboratory of Neuro-immunology.

There are many parallels or analogies between these NINDS-supported studies on slow or latent viruses in the central nervous system and the work being done on tumor-producing viruses by the National Cancer Institute. We have achieved considerable coordination of the interests of NINDS and NCI and this will intensify as the facility assigned to NINDS at the Frederick Cancer Research Center is renovated and brought on line next year. I am pleased to acknowledge here the generous spirit of cooperation that we in NINDS have enjoyed with NCI.

Neurobiology is today at the center of the most challenging unsolved problems of biology. From the laboratory bench to the hospital bedside, the investigators supported by NINDS confront these challenges at one of man's last great frontiers—the frontier of the nervous system. We are now entering an era in which I believe we will see the great unconquered bastions of neurological and communicative disorders crumble, so that the quality of human life in this country and in the world will no longer be in jeopardy.

In conclusion, Mr. Chairman, the budget request for NINDS for 1975 is $119,958,000.

I thank you for the opportunity to appear before you, and I shall be pleased to try to answer any questions and to supply additional information desired for the record.

UNFUNDED GRANTS

Mr. Flood. I note that in fiscal year 1975 you expect to have $36,574,000 worth of approved but unfunded research grants, whereas in 1974 you will have only $9,577,000 in approved but unfunded research grants.

What accounts for that very large increase in unfunded research grants?

Dr. Tower. This is largely explainable, sir, by the additional moneys made available through the release of the 1973 funds which have been obligated in 1974, so we tend to have a peak, and then come back down to the levels where we were both before and after.

Mr. Flood. How do you know that you will have so many unfunded applications in 1975? Have these applications already been received? Do you have them?

Dr. Tower. This is an estimate, sir, based on our past experience, of the numbers of applications that will come in. One can draw projection curves and get a pretty close estimate. We find our estimates are within 5 or 10 percent.

Mr. Flood. Does the fact that there will be such a very large number of unfunded research applications indicate that there is a very large pool of talent not being utilized at all?

Dr. Tower. Yes, sir.

Mr. Flood. Does that indicate, then, that there are too many trained researchers around?

Dr. Tower. No, sir. We have a lot of problems still to solve.

Mr. Flood. You want it both ways, huh? What happens to the people whose applications are not funded? In other words, what do they do, instead of research?

Dr. Tower. Mr. Chairman, let me answer the question in part this way, because we have had a little experience——

Mr. Flood. I'll bet.

Dr. Tower [continuing]. With the effects of the release of the 1973 funds. We have had to go back and find out, on those grants which were approved but not funded and now could be funded with the released 1973 funds, whether the investigators are still in business and are still eligible for those grants.

In most cases the answer is, yes, they are in business and they are eligible for the grants in terms of carrying on the same type of work, but we found that a quite surprising number had obtained support elsewhere, usually in the private sector, or had gone into other activities—not a large percentage, but more than we had anticipated.

Mr. Flood. Does one investigator send in many projects, knowing that many of them will be refused anyhow?

Dr. Tower. Not usually.

Mr. Flood. No?

Dr. Tower. They repeat. Once they are approved but not funded, they will come in again.

AVERAGE COST OF NEW GRANTS

Mr. Flood. Take a look at the table you have on page 232 of your justifications. That indicates the average cost of a new project will drop from $39,000 in 1974 to $18,000 in 1975. How do you explain that? There it is.

Dr. Tower. You are looking at the new grants?

Mr. Flood. New grants, yes.

Dr. Tower. In 1974, there was a fairly sizable number of large center and program project grants funded as new grants which are not anticipated in 1975. That will explain largely the difference in those figures.

Mr. Flood. Is it not likely the figures are incorrect? The average cost of a research project has been increasing every year for as long as anybody around here can remember. Wouldn't that indicate those figures are wrong?

Dr. Tower. I think you will find we have some very large grants in there which would be nonrecurring. In other words, we funded some large grants in 1974, and we do not anticipate we will have those again in 1975.

Mr. Flood. You had better take a look at that for the record.

Dr. Tower. Mr. Chairman, we will check it and send you a statement.

[The information follows:]

The table of regular research grants for 1975 on page 232 of the estimate incorrectly reflects the programs for competing and new grants.

The following table is the Institute's new estimate for the distribution of these grants in 1975:

[In thousands of dollars]

Research grants	1974 as printed			1975 revised		
	Number	Amount	Average	Number	Amount	Average
Noncompeting	622	$36,468	$58.6	721	$47,579	$65.9
Competing	377	21,884	58.0	178	10,496	59.0
New	232	9,035	38.9	227	10,230	45.1
Supplemental	(100)	1,294	12.9	(95)	1,250	13.2
Total	1,231	68,681	55.8	1,126	69,555	61.

COORDINATION OF RESEARCH EFFORTS

Mr. Flood. We touched upon this earlier with the other Institutes. Can you explain the division of responsibility between your Institute and the Heart and Lung Institute with respect to research on strokes?

Dr. Tower. I think the division is quite clear. We have had a continuing dialog between the two Institutes because we have a joint subcommittee to our two advisory councils to deal with this particular problem.

The Heart Institute has as its primary focus in this area the problems of high blood pressure, arteriosclerosis, and the things which affect the body generally. The major complications of these pathological conditions is stroke or heart disease. A person who has these has two strikes against him. He is going to have a heart attack or a stroke in most cases.

The Heart Institute deals with the heart attacks, and we deal with the strokes. Because nobody else wants to deal with it, the neurologist is left with the problem of dealing with stroke.

We think it very important, not only because of the large number of people involved, but because it presents a very important problem for us to solve.

Dr. Stone. You brought this question up earlier as you yourself indicated, and Mr. Conte has. He and I had a brief conversation about it. On that account, if I have your permission, I will talk very briefly about it.

As I said on another occasion in this hearing, we have asked Dr. Stetten to take responsibility for integration between the Institutes. The Institutes already do a splendid job of this. They are very alert for possibilities of related findings in other fields.

We also examine this matter very carefully and are constantly alert to it. It is a reflection of the fact that the human body is all one piece of tissue. Human biology is all connected. Virtually every disease affects another disease. Research at the most basic levels of the body involves all of the various systems. So, we are alert to it and we appreciate the opportunity to comment on it.

STROKE

Mr. Flood. You point out that stroke is the No. 3 killer in the Nation; and that of the 2.5 million survivors, 55 percent require very special care.

Do you know anything about how to prevent strokes? Have we learned anything new recently about this?

Dr. Tower. We know if you can control the blood pressure, this is a major factor in preventing stroke. It is estimated that you may prevent as many as 50 percent of the strokes by controlling the hypertension.

We also know that there are special situations—diabetes is one which you were discussing a little earlier with the previous Institute—in which stroke is a complication. So, effective control of diabetes, for example, is another way of going about it.

There will always be some stroke patients because we have a certain number of the total population in which there are abnormalities of the blood vessels in the brain. These are usually developmental abnormalities which a person is born with, and later on they show up and blow out and produce a stroke.

Until we know how to diagnose these ahead of time and until we have the techniques for dealing with them once we can diagnose them ahead of time, we will have a certain number of these to contend with.

The major push right now is for controlling high blood pressure. This will greatly reduce the number of stroke patients.

Mr. Flood. With respect to the treatment of stroke victims, do you believe a large proportion of these people are not doing as well as they ought to because they simply do not have access to the most up-to-date methods of treatment and rehabilitation?

Dr. Tower. It is difficult to answer that question absolutely, sir.

Mr. Flood. I know it.

Dr. Tower. As I pointed out, we have 16 stroke centers and 11 stroke acute care research units that provide what we believe is the optimal care for stroke patients at this time. These people do very well, but we have not yet ascertained that they necessarily do better than those people who get care in other centers or who get relatively little care.

I think this is a point on which we need to obtain more information. That is the reason I am a little hesitant to answer your question in an absolute way. I know what you are getting at.

Mr. Flood. So do I.

Dr. Tower. I do not think we have the answer to your question.

Mr. Flood. All right.

Along that line, should we be doing more to disseminate information about treatment of stroke victims?

Dr. Tower. Yes, sir.

Mr. Flood. Do you see this as a proper role for your Institute?

Dr. Tower. We had a commission look into this matter, and they brought in a report last year. We are in the process of boiling down the information and the recommendations which that commission made, to two types of information we can put out.

One is a pamphlet for the general physician, the general practitioner, who may not be aware of all the latest advances in the stroke area. We would like to be able to make this available to him generally.

The other is to be put out in some journal, like Science, for example, to make the scientific public in general aware of what the commission found and what its recommendations are.

Mr. Flood. It is your job. If you had said it was not your job, I was going to ask whose job it is.

Dr. Tower. It is our job, and we are in the process of doing it.

HEAD AND SPINAL CORD INJURY CENTERS

Mr. Flood. Will you please list the four head injury clinical research centers, the five acute spinal cord injury clinical research centers, and the four spinal cord injury program projects, with the dollar amounts allocated to each one of them for 1974 and 1975?

Dr. Tower. Yes, sir.

[The information follows:]

[In thousands]

	1974	1975
Head injury clinical research centers:		
1. University of Cincinnati, Cincinnati, Ohio	$127	$129
2. New York University, New York, N.Y.	150	150
3. University of Chicago, Chicago, Ill.	204	204
4. University of Pennsylvania, Philadelphia, Pa.	396	254
Acute spinal cord injury centers:		
1. St. Joseph Hospital and Medical Center, Phoenix Ariz.	178	259
2. New York University, New York, N.Y.	592	480
3. Ohio State University, Columbus, Ohio	444	460
4. Yale University, New Haven, Conn.	868	852
5. Medical University of South Carolina, Columbia, S.C.	291	270
Individual research grants emphasizing spinal cord injury:		
1. University of North Carolina, Chapel Hill, N.C.	250	274
2. Washington University, St. Louis, Mo.	90	84
3. Hahnemann Medical College and Hospital of Philadelphia	133	133
4. University of North Carolina, Chapel Hill, N. C.	85	79

SPINAL CORD INJURY TRAINING PROGRAM

Mr. Flood. Have you considered incorporating a training program in the spinal cord injury centers so physicians and nurses and even paramedics could go there for short periods of time to learn your most advanced methods of treatment? Would that not be desirable?

Dr. Tower. Yes, sir. As a matter of fact, this is being done, perhaps not on a formalized basis as you have presented it as a training program, but each one of the spinal cord injury centers has built into it the importance of training——

Mr. Flood. What about a training program?

Dr. Tower. Yes, sir.

Mr. Flood. That almost answers itself. There is the center. Here they are.

Dr. Tower. We are already doing this informally, but we could certainly expand it, yes, sir.

Mr. Flood. Look at this from the standpoint of a training program. You are all set up. Also, would something similar be desirable in the stroke centers and the head injury centers?

Dr. Tower. These are already going on in the informal sense without announcing a specific program. There is a great deal of training going on.

Mr. Flood. I am talking about a training program.

Dr. Tower. May I say, Mr. Chairman, I think where we have the spinal cord centers, particularly in those areas, many people have come and a great deal of the information is already disseminated, not only to the physicians, but to the rescue squads, the nursing groups, and so on.

Mr. **Flood**. Good. Take a look at the idea of setting up a training program in all those areas where the centers are. Such a program seems to be vital.

MULTIPLE SCLEROSIS

Summarize briefly for us the recommendations of the National Advisory Commission on Multiple Sclerosis. Tell us something about that, and then for the record you can develop it at some length.

Dr. **Tower**. Yes, sir.

Mr. **Flood**. A lot of people will look at that.

Dr. **Tower**. Yes, sir.

We have prepared a position paper, actually, for the guidance of the Department. We will be glad to supply you with a copy of this. It is a very brief overview of the recommendations.

[The information follows:]

MEMORANDUM DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH

TO : The Assistant Secretary for Health, DHEW DATE: March 25, 1974
Through: ES/PHS
Through: Director, NIH

FROM : Acting Director, National Institute of Neurological Diseases and Stroke, NIH

SUBJECT: Analysis and Comments on the Report and Recommendations of the National Advisory Commission on Multiple Sclerosis--INFORMATION

Background

The National Advisory Commission on Multiple Sclerosis was established by PL92-563 which was signed by the President on October 25, 1972.

The Commission was charged with determining "the most effective means of finding the cause of and cures and treatments for multiple sclerosis" and giving particular emphasis "to the need for additional financial support by the Federal Government and the means by which the Federal Government can best participate in" this effort. The Commission was directed to "transmit to the Secretary, DHEW, for transmittal to the President and the Congress, a final report."

The Commission was chaired by Mr. Charles W. V. Meares and was composed of 12 members, four of whom were members of the NANDS Council. To help accomplish its task, the Commission with the approval of the Secretary, DHEW, created an ad hoc advisory committee of 53 physicians and scientists. This advisory committee was formed into seven working groups on clinical studies, virology, immunology, pharmacology, biochemistry, epidemiology and pathophysiology.

The Commission's report in two volumes and dated February 11, 1974, was presented to the Secretary, DHEW, on February 18, 1974. Volume One of the report, comprising some 67 pages presents an overview. Volume Two totalling 374 pages documents the detailed reports of the seven working groups formed from the ad hoc advisory committee. In the following comments we deal principally with the overview in Volume One.

Recommendations

The Commission has recommended support for both basic (fundamental) research in the neurosciences and target- or disease-oriented research aimed at problems relating specifically to multiple sclerosis (MS). The Commission estimated the current total

Federal funding in these two categories to be $31.5 million and $3.15 million, respectively. The Commission proposes additional funding for the next three fiscal years as follows (in millions of dollars):

	FY 1975	FY 1976	FY 1977
Additional research specific to MS	$3.86	$5.84	$7.0
Additional basic research in neurosciences	12.015	12.45	12.9
TOTALS	15.875	18.29	19.9

The basis for these dollar recommendations are summarized on pp. 54-55 of Volume One of the report.

General Recommendations

*A. Establish three more MS Clinical Research Centers (recommendation #1; proposed FY '75 funding: $750,000).

Comment: The NINDS has been funding two centers (at UCLA and at Univ. of Pennsylvania-Wistar at a FY '73 level totalling $1.1 million). A third center (at Emory Univ.) has been awarded in FY '74 ($0.22 million) as the first of the three recommended by the Commission.

*B. Improve management of MS research program by designating a medical scientist as focal point within the NINDS to maintain liaison with the biomedical community and other Federal agencies with respect to MS research (Vol. One pp. 57-58; recommendation #31; proposed FY '75 funding: $39,000 for data bank).

Comment: The Acting Director, NINDS, has designated Dr. John L. Sever, Chief, Infectious Diseases Branch, Collaborative and Field Research, NINDS, as the Institute focal point for MS research and as head of an MS Task Team of NINDS scientists.

C. Appoint a multidisciplinary study section on multiple sclerosis (Vol. One pp. 58-60).

Comment: In our opinion the review of research grant applications relevant to MS can be adequately accomplished by regular NIH Study Sections already in existence. For the technical merit review of MS contracts proposals, we already have access to outstanding authorities in scientific areas relevant to MS.

D. Promote communication and collaboration by sponsoring bench-and-bedside workshops. (Vol. One p. 27.)

E. Give more meaningful attention to the economic and social plight of MS patients. (Vol. One, pp. 60-67.)

Comment: These considerations relate to needed administrative and legislative measures in the Medicare-Medicaid, Social Security, Veterans, and private insurance sectors.

Specific Recommendations

1. Develop specific diagnostic tests for MS and measures to evaluate stages of the disease (index of progression) and "trigger" mechanisms (predictive changes). (Recommendations #8, 9, 25; proposed FY '75 funding $260,000.)

2. Establish mechanisms for providing fresh tissue samples from MS patients for virological and immunological research studies. (Recommendation #2; proposed FY '75 funding $60,000.)

3. Promote approaches to therapy of MS: (a) immuno-therapy; (b) therapy for disturbances in nerve conduction and synaptic transmission; (c) establishment of a comprehensive MS treatment center for problems of spasticity, pain, muscle weakness, bladder dysfunction and infections, bedsores, etc. (Recommendations #10, 11, 14, 15; proposed FY '75 funding $575,500.)

Comment: Workshops designed to develop such approaches, as proposed by the Commission, seem to us essential here. Whether a treatment center (c), separate from the clinical research centers, is necessary or desirable is questionable in our opinion. We would expect that the three existing and two proposed clinical research centers could incorporate such problems into their programs.

*4. Conduct various epidemiological studies: (a) geographical and cluster foci (in the USSR and the Shetland-Orkney Islands); (b) prospective (optic neuritis and measles vaccine groups); (c) retrospective (in recently diagnosed cases). (Recommendations #13, 17, 18, 26-28; proposed FY '75 funding $410,000.)

Comment: Plans for the Shetland-Orkney survey are in final stages of contract negotiation by the NINDS.

*5. Underwrite major programs in virological research: (a) attempts to isolate viruses from MS tissue samples; (b) cell culture studies; (c) antigen-antibody studies; (d) virus-cell membrane interactions. (Recommendations #3-7, 20-22; proposed FY '75 funding $1,318,000+.)

> Comment: This is one of the two major research areas favored by the Commission for high priority. Experts in the field believe MS is most likely to be a virally related disease. The NINDS has a very strong on-campus team working in all four of the areas specified, supplemented by additional collaborative and grant-supported studies. In our opinion even more research should be promoted in these areas. Special training and fellowship programs in neurovirology have been inaugurated by NINDS.

*6. Promote major research into immune mechanisms: (a) reinvestigation by modern techniques of immune reactions in the central nervous system; (b) studies on the significance of IgG in the CSF; (c) clarification of the serum-induced demyelination phenomenon; (d) testing at the Clinical Research Centers for humoral and cellular immunity. (Recommendations #12, 16, 19, 23, 24; proposed FY '75 funding $445,000.)

> Comment: This is the other major research area favored by the Commission for high priority. Much circumstantial evidence focuses on immune mechanisms as major factors in MS. The NINDS has already proposed to establish an intramural Laboratory of Neuro-immunology and is recruiting for its chief. Special training and fellowship programs in neuro-immunology have been inaugurated by NINDS. In our opinion this is a crucial area warranting special emphasis.

7. Encourage development of animal models for MS. (Recommendation #29; proposed FY '75 funding $25,000.)

General Comments

In general the NINDS staff concurs in the findings and recommendations of the Commission. In our opinion the justifications for most of the recommendations are valid, and the modest proposals for funding lend further credibility to the seriousness and depth of study which the Commission brought to its task. As indicated above by comments, for the items asterisked (*), the NINDS has already initiated some degree of implementation. The Commission urges (Vol. One, p. 11, top) that any funds specifically appropriated for MS research which cannot be expended within a given fiscal year ought to revert to the Treasury rather than being diverted to some other program. In our opinion such restrictive earmarking could tie the hands of the Director, NINDS, unnecessarily.

The NINDS concurs with the National Advisory Commission's belief that the time is ripe for a concerted, adequately financed and well-managed effort aimed at the elucidation of MS. In the words of the Commission, there are now sufficient promising leads for scientists in many disciplines to pursue, given the opportunity and requisite support, that will produce substantial gains for MS victims and for society as a whole in the near future. To this end, we believe that the Commission has been exceptionally responsible in recommending a balanced program of both basic research in the neurosciences and targeted or MS-oriented research.

Donald B. Tower, M.D.

Dr. Tower. I think these can be summarized into two major subdivisions, some very general recommendations such as establishing some more clinical research centers, establishing a focal point within our Institute, promoting more communication by sponsoring workshops, and that sort of thing.

These are general recommendations.

I might say that we have already funded an additional clinical research center at Emory University in Atlanta. That makes one of the three that the Commission recommended. We have established a focal point within the Institute. Dr. John Sever will serve as that for the research community.

There are a number of specific recommendations which we have summarized in seven groups. I will not talk about all of them because I will put them in the record, but certainly I can say we are already in business in a few of them to a partial degree.

In epidemiological studies, which is one of the major areas that the Commission recommended, we are in the process of planning for a survey in the Shetland-Orkney Islands, which have the highest incidence of multiple sclerosis of any place in the world. That is almost at the finalization stage for the contract.

We have a number of studies going on in both virological and immunological areas which represent the nucleus for promoting more work in these areas. I think these are the important areas. I think this is where the answers lie.

PERINATAL PROJECT

Mr. Flood. Is the collaborative perinatal project finished now?

Dr. Tower. Not quite. It has one more year to go.

Dr. Flood. What has been the total cost to date, and how long will it take to analyze the data?

Dr. Tower. The gentleman will give me the total cost in a minute. The data are being analyzed now.

Mr. Flood. How long will it take?

Dr. Tower. We expect to have that completed pretty much by 1976.

Mr. Flood. Have you any dramatic findings so far, anything that stands out like a sore thumb?

Dr. Tower. We have had a few dramatic ones, like the demonstration of the effect of German measles at a certain stage in pregnancy, and the development of a vaccine which will prevent many of those complications from occurring.

Mr. Flood. Can you tell us whether or not this was a worthwhile investment?

Dr. Tower. Yes, sir, I think it was a worthwhile investment. The total number, sir, is $116 million, approximately, for the whole project over a period of roughly 15 years.

ACTING DIRECTOR

Mr. Flood. I would like to ask Dr. Stone this question:

It has been a long time since we had a Director for this Neurological Institute. We have had an Acting Director. Can you tell us when we will have a change in that situation?

Dr. Stone. Yes, sir. More than a month ago we nominated Dr. Tower to be permanent Director. That is going through the mechanics now. As far as I know, there is no problem in that at all, except merely getting the paperwork done.

SPECIAL REPORTS

Mr. Flood. For the record, I want the usual special reports on some of the diseases that you study in your shop.

We would also like a special report on Huntington's chorea and Meniere's disease. There has been a lot of interest in those very recently, as you know. Make a special report on those two.

[The information follows:]

STROKE

Stroke (cerebrovascular disease) is the third largest cause of death and the leading cause of long-term disability in the United States. Each year about 500,000 Americans are stricken, and about 200,000 die. There are about 2 million stroke survivors in the country, with varying degrees of disability. This year an official Commission on Stroke estimated that 30 percent of stroke survivors recover sufficiently to return to work or to their normal activities; 55 percent have their lives impaired, but are able to carry on the activities of daily living, often with help; and 15 percent become completely incapacitated and are so helpless that total nursing care is required for the rest of their lives.

No detailed estimates of the losses sustained by victims of stroke can be made with available data, but the Commission proposed a figure of $1.2 billion per year excluding physician services and non-hospital care. Estimates by other groups have gone as high as $4 billion in total cost to the Nation. Lives are stunted or effectively ended; families disrupted or impoverished for months or years; valuable contributors are lost to society. There are thus immense benefits to be achieved through research in this field--in both monetary and human terms.

The Department's activities in cerebrovascular disease are conducted by the National Institute of Neurological Diseases and Stroke (NINDS), and the National Heart and Lung Institute (NHLI) of the National Institutes of health.

Obligations for programs in stroke (cerebrovascular disease)

	1971	1972	1973	1974 estimate	1975 estimate
National Institutes of Health:					
National Institute of Neurological Diseases and Stroke.	$5,784,000	$6,791,000	$6,983,000	$11,463,000	$9,902,000
National Heart and Lung Institute......	1,500,000	1,664,000	2,277,000	2,430,000	3,600,000
Subtotal, National Institutes of Health.	7,284,000	8,455,000	9,260,000	13,893,000	13,502,000
Health Resources Administration:					
Regional Medical Programs Service....	5,499,000	4,192,000	1,538,000	---	---
Total.............	12,783,000	12,647,000	10,798,000	13,893,000	13,502,000

NATIONAL INSTITUTES OF HEALTH

National Institute of Neurological Diseases and Stroke

A stroke is a sudden loss of brain function resulting from interference with the blood supply to the brain. It is often the culmination of progressive cerebrovascular disease, which may extend over many years, and which may not be readily detectable. Some strokes are minor episodes, while others may cause death in a few minutes. Usually they are brought on by one of four events: thrombosis--a clot within a blood vessel of the brain or neck; cerebral embolism--the blocking of a blood vessel in the brain by a piece of clot or other material carried through the circulation from some other part of the body; narrowing (stenosis) of an artery supplying blood to the brain; or cerebral hemorrhage--the rupture of a cerebral blood vessel with bleeding into the brain tissue.

An important underlying cause of cerebrovascular disease is atherosclerosis. In atherosclerosis, fatty deposits form within the inner lining of an artery wall and decrease the size of the channel carrying blood to the brain. Also, material from the deposits may break off and cause blocking of one of the cerebral arteries. High blood pressure (hypertension) has also been shown to be associated with a considerable increase in the frequency and severity of vascular diseases of the brain, especially cerebral hemorrhage. Among other causes of stroke are aneurysms, and abnormalities in the clotting process. Aneurysms are sac-like swellings which may rupture, and are usually caused by congenital weaknesses in the artery walls. Abnormalities in the blood clotting mechanism may result in spontaneous hemorrhage.

Whatever the specific process involved, interference with the blood supply to the brain for more than about five minutes inevitably leads to death of some brain cells and impairment of function. Temporary or permanent paralysis of movement, thought, memory, speech or sensation is the result.

Although the event of a stroke can be described in simple mechanical terms, cerebrovascular disease as a whole poses an extremely difficult set of medical, scientific and technical problems. The brain is an incredibly complex structure, with billions of delicate nerve cells and myriad interconnections and pathways. The circulatory system providing for its nutrition is correspondingly complex and delicate. Also, the brain and its supporting systems are placed within the relatively inaccessible bony skull. Scientists trained in many branches of biology and physics, as well as physicians skilled in clinical practice, must work closely together if cerebrovascular disease is to be well enough understood for man to intervene and prevent or cure it.

The NINDS Program

In the past 10 years there has been a substantial increase in scientific and medical interest in cerebrovascular disease. This has been brought about in large part by the growth of the NINDS stroke program: in Fiscal Year 1973, Institute support for research in stroke reached a level of approximately $7 million, representing 37 research project grants, 15 clinical research centers, and 10 acute care research units. Additional support was provided for training in neurology and other related disciplines, as well as through support of meetings and publications.

A small research program is conducted at the Institute in Bethesda, Maryland. At present this includes a study of non-acute cerebrovascular disease in young patients (up to 40), and animal studies aimed at possible salvage of some brain tissue after a stroke. Also, the Institute has recently established a Section on Head Injury and Stroke within its Collaborative and Field Program. This unit has begun sponsorship, through contracts, of a large statistical study of the hospital frequency and characteristics of transient ischemic attacks (little strokes). This study, which is in progress at six centers, is expected to run for three years and provide data on approximately 1,000 patients.

Commission on Stroke

In early 1972, NINDS established a Commission on Stroke, composed of 12 leading experts in the field, to survey the status of the national stroke effort. This Commission reviewed what is known about all aspects of stroke, focused on measures urgently needed during the next several years, and made recommendations in order of priority. The Commission's report, entitled "A Blueprint for National Action Against Stroke," was completed in March of this year, and is available from the Institute.

Clinical Research Centers

Cerebrovascular clinical research centers, located in large university medical complexes throughout the country, now make up the largest segment of the program. These units, most of which are multidisciplinary, are staffed by as many as 15 to 20 scientists and physicians, plus technicians and other assistants. They vary in approach, some concentrating on single research areas, as at The Johns Hopkins University, where the epidemiological aspects of stroke are being studied. These include studies of incidence and prevalence, methods for early detection of "high risk" segments of the population, familial aggregation of stroke cases, and similar questions. A center at Boston University devotes its efforts entirely to research in aphasia, a speech disorder which often follows stroke.

Other centers are broader in focus, often working with several approaches, such as the physical dynamics of blood flow, brain metabolism, pharmacology, surgery, the development of better methods of diagnosis and treatment, and many others. Generally the centers have interrelated clinical and basic research programs, and have accommodations for up to 30 research patients. All of the centers also conduct training programs for young physicians, scientists, and other staff members.

Project Grants

In addition to the team efforts of the clinical research centers, smaller research projects are being conducted with Institute support. These range from basic laboratory studies in such fields as neurophysiology and biochemistry to clinical investigations of drug effectiveness, improvement of diagnostic devices and techniques, and development of improved surgical and medical approaches. These smaller projects often provide information which is later exploited by the larger teams in the stroke research centers.

Collaborative Studies

One type of study which NINDS uniquely is able to sponsor, by reason of its resources and central role, is the cooperative study--the large-scale gathering and analysis of data from groups of institutions, using uniform definitions and methods. In this way, valid statistics can be produced and used as the basis for choices in research planning, and for improvements in treatment.

NINDS has sponsored several large cooperative studies in cerebrovascular disease. The most recent of these has been a study of patients in eight medical centers aimed at showing whether antihypertensive drug therapy reduces incidence of second strokes, as it does in the case of initial strokes. The results clearly show that the therapy does not decrease the risk of another stroke, and have thus provided valuable new guidelines for physicians treating these patients.

Other Groups Working in the Stroke Field

Several other components of the National Institutes of Health support some research relating to stroke, including the National Heart and Lung Institute (NHLI). NHLI's basic programs in atherosclerosis and hypertension research, aimed at elucidating the fundamental mechanisms of these disorders, make up a major portion of its total effort. A meaningful figure covering all of this work bearing a possible relation to cerebrovascular disease would be difficult to provide, but the more directly stroke-related projects total about $2.4 million annually. Also within the Department of Health, Education, and Welfare, the Social and Rehabilitation Service (SRS) provides help to stroke victims. SRS provides grants for the training of rehabilitation workers, and approximately 7,200 stroke patients per year receive rehabilitation services through SRS funded state programs. The Veterans Administration, through its 168 hospitals, provides medical services to many of the 28 million veterans in the U.S., and admitted 13,685 stroke patients to its hospitals in Fiscal Year 1972.

Outside of the Federal Government, two national voluntary associations, the American Heart Association and the National Easter Seal Society for Crippled Children and Adults, have substantial interests in cerebrovascular disease. Seventeen out of 55 American Heart Association local chapters had stroke programs in 1970, and the national office provided some $68,000 for research grants. The Easter Seal Society affiliates spent some $3.2 million in 1970 for stroke, principally for direct service to patients. The National Health Education Committee, although it has no funds for services or research, operates a public information program in this field.

Large hospitals, medical schools, health departments, and hundreds of other institutions throughout the country provide stroke services or operate local programs benefiting stroke patients, but the entire national effort, individual and collective, is most inadequate in view of the size of the problem.

Stroke Research

Diagnosis

Stroke diagnosis, on which treatment obviously depends, is still an inexact science. It is of at least equal priority with treatment in the NINDS research program, and a substantial effort is being made to find better methods, and to refine and improve existing ones. The best of the present methods, X-ray angiography, involves injection of radioopaque dye into the neck arteries and subsequent X-ray examination of the head. The procedure, however, carries some risk of reaction to the dye, and the films are difficult to interpret because of the complexity of the circulation, and the problem of depth perception. Solution of the latter is being attempted through the technique of X-ray tomography, or focusing of the picture on a specific section, or plane, within the head. Most of the work in angiography has been devoted to a search for better dyes, and an effort to improve the technical quality of the films.

Many other methods have been tried, including injection of radioisotopes and subsequent scanning with a radiation counting camera; ultrasound projection and translation of the echoes into a picture; recording of bruits, or abnormal sounds in the neck arteries; examination of retinal arteries; minute measurements of heat patterns radiating from the face, and various others. Except for the isotope scan, however, all of these methods are too limited to be used extensively in clinical practice.

A new diagnostic technique, computerized soft tissue tomography, has been hailed by a prominent radiologist as "probably the most important advance in radiology in 50 years." The technique, first developed by an English company, EMI, Ltd., and embodied in a scanning instrument, employs a narrow beam of X rays to rapidly scan the patient's head in a series of thin slices. The beams pass through the head and hit two crystal detectors which feed signals into a high speed computer. At each of 28,000 points along the scan, the computer calculates the difference between the X rays originally emitted and those received on the crystals--the absorption coefficient--of the intervening tissues, blood, and bone. The computer also produces an oscilloscope picture for immediate viewing or photographic recording. Two patients per hour can be scanned. The equipment is sensitive enough to detect differences in absorption of only one digit in a scale from -500 (air) to +400 (bone), and has so far been used to find cysts, neoplasms, abscesses, cerebral infarcts, intracerebral hemorrhages, and the plaques of multiple sclerosis. It is considered to be 100 times more sensitive than conventional X-ray diagnosis, and may well make the older methods obsolete, especially the "invasive" ones which involve injection into the body of dye, radioisotopes, or air.

In November 1973, two EMI scanners were operational in the United States, one at the Mayo Clinic and one at Massachusetts General Hospital. Both institutions are sites of Institute-supported stroke centers. A number of others are on order by other institutions, including the National Institutes of Health, with installation at NIH expected by spring or early summer, 1974. The NIH instrument is being funded jointly by NINDS, the National Cancer Institute, and the Clinical Center.

Treatment

Progress in treatment of cerebrovascular disease is based on many small but steady improvements rather than any single striking changes. Treatment varies according to the stage of the illness and the type of vascular problem encountered. No one new procedure or development is expected to affect the prospects for all patients, but a few provide a sense of the generally optimistic climate.

Surgery

For many years cerebrovascular surgery has been limited almost entirely to correction of flaws or blockages (aneurysms, malformations, etc.) in the larger arteries. The carotid arteries in the neck are relatively accessible, and the larger intracranial arteries have become more so in recent years. The operating microscope has made it possible for the neurosurgeon to operate directly on smaller vessels in the brain. Clots can now be removed from very small blood vessels, and also very small blood vessel grafts can be made to by-pass aneurysms and provide collateral circulation. Some of the most productive work in this field has been reported from NINDS-supported research teams such as the group at the Mayo Clinic in Rochester, Minnesota.

In one report this year, Mayo neurosurgeons described monitoring methods employed during 81 carotid endarterectomies (an operation for "reaming out" a clogged neck artery). They found a high correlation between cerebral blood flow and alterations in the patient's electroencephalogram, or EEG (brain wave recording). They also found that the degree of EEG change accurately reflected the severity of flow reduction, but was always reversible with the placement of a shunt (by-pass around the obstruction). The investigators concluded that the EEG is a valuable monitoring aid in this operation since it indicates to the surgeon when a shunt is required and reflects the state of cerebral function not only during occlusion but also throughout the surgical procedure.

The importance of having good experimental models for the study of cerebrovascular disease has long been recognized. Cerebral ischemia (constriction) and infarction (blockage) can be produced in some small animals by tying or clamping a middle cerebral artery. However, most surgical approaches to the artery require removal of part of the cranium, and this introduces complicating elements including edema and decompression. Grantees at the University of Minnesota reported that they have developed a transorbital (eye socket) approach which can be sealed immediately after occlusion of the artery. They found this is a superior experimental model for many studies.

On the less optimistic side, the skills required to perform such delicate surgery are in short supply, and criteria for selection of possible surgical candidates are not universally agreed upon. Also, relatively few patients have operable forms of cerebrovascular disease. It thus seems unlikely that brain surgery, however perfected and refined, will have a substantial impact on stroke statistics in the near future.

Drugs

An intense search continues for better drugs for treating cerebrovascular disease. Anticoagulants are commonly used in non-hemorrhagic strokes, as are blood-pressure-lowering agents. Efforts are being made to evaluate clot-dissolving (thrombolytic) agents, and drugs that relax the brain blood vessels and allow them to open to their fullest diameter (vasodilators).

Drugs that reduce the tendency of blood cells to stick to one another, including one of the most familiar drugs in existence--aspirin--are being increasingly studied. This year Institute grantees at Indiana University School of Medicine corroborated recent evidence that aspirin may be helpful in some cerebrovascular cases. In one investigation, 20 dogs were treated with aspirin or placebos prior to and following experimentally induced arterial thrombosis. Clots were found in 36 percent of those treated with placebos, but in only eight percent in those treated with aspirin.

The investigators also studied 26 patients who had suffered from transient ischemic attacks (little strokes). Fifteen were treated with aspirin and eleven were not. No difference in death rate was noted, but only two of those treated with aspirin had another transient ischemic attack, compared to nine of those who had no aspirin. The numbers of patients are too small and the conditions too limited for aspirin to be considered a standard treatment at this point. However, continued research on aspirin and similarly acting drugs, such as sulfinpyrazone and dipyridamole, is clearly indicated.

Negative results with drugs are often as important, from a research standpoint, as successes. Patients benefit, and scientists find new insights and are able to avoid blind and even dangerous alleys. For example, the steroid drug, dexamethasone, has shown consistently good results in treatment of the brain edema, or swelling, accompanying gliomas (brain tumors). This led to the assumption that it might also be helpful in reducing the edema accompanying some strokes. Two studies this year of trials with dexamethasone, one by scientists at Wayne State University School of Medicine, and the other by NINDS grantees at the Mayo Clinic, were completely disappointing therapeutically, in both animals and humans, but the data published will be of considerable value to clinicians and basic scientists in the future. Similarly, another group of investigators found that promising results of treatment with an anticlotting drug, aminocaproic acid, in hypertensive patients, are negated if antihypertensive therapy is concurrently instituted.

Anticoagulants, which have been in use for many years, still present a complex evaluation problem. In a recently reported grantee study of anticoagulants used in treating little strokes, data were gathered on 198 patients whose illnesses were followed for 14 years. Subsequent strokes occurred in 19 percent of the treated patients and 40 percent of those who were not treated. At one, three, and five-year points after the first attack, there was no significant difference in survival, but the incidence of stroke was significantly less in the treated patients.

Acute Care Research Units

Since 70 to 80 percent of stroke mortality occurs within the first 10 days, and since the outlook for survivors depends heavily on the quality of care during the acute phase of the crisis, the need for better "acute care" is obvious and urgent. In March 1973, the Institute funded new acute care research units in the medical centers of 10 universities: Iowa, Virginia, Utah, Johns Hopkins, Wake Forest, Michigan, Ohio State, Alabama, Rochester, and Loma Linda. These units are being equipped for precise monitoring of vital signs and levels of body function, and will strive to find ways of preventing small strokes as well as treating the acute phases of major strokes. They will resemble the intensive care units that have been so successful in managing coronary disease, except that they will be oriented toward research on the brain, and will provide a vital training resource for physicians, interns, and ancillary personnel.

Epidemiology

Statistical studies of cerebrovascular disease in large groups of people hold potential of finding causes and the enormous rewards that would come from large scale prevention.

The Institute is supporting several epidemiological studies, in addition to the Johns Hopkins center devoted entirely to this work.

The question of familial incidence, and possible hereditary factors, has tantalized scientists for years. Two studies reported this year, one from England, and one by NINDS grantees, suggest the conclusion that close relatives of cerebrovascular patients are at no greater risk than unrelated persons. The English study, limited to hemorrhage and to the brothers and sisters of 180 patients, found no statistically significant excess of deaths. In the grantee study, the families of 80 patients were studied, together with predisposing illnesses, including hypertension, diabetes, and heart disease. No independent inheritance of cerebrovascular disease was found in this group either, and the investigators have concluded that the belief that stroke "runs in families" has been substantially weakened.

U.S. mortality from stroke is considerably higher among Blacks than among Caucasians, the Blacks having a rate of approximately five deaths per 1,000 population at age 60, with the Caucasians showing a rate of only around one death per 1,000 at that age. Other studies have indicated that in most industrialized countries Negro ethnic groups have illness and death rates several times higher than Caucasian populations, but whether these high rates are due to genetic or environmental factors is unknown.

An NINDS-directed study begun this year in Panama may throw some light on this question. An unusual opportunity exists in Panama to study several geographically distinct Negro populations living in different environmental situations, without encountering the high mobility and rapid urbanization factors which complicate studies in the U.S. The Panamanian populations include two groups of descendants of West Indian Negroes brought to Panama as laborers on the Canal between 1880 and 1913, one living a typical westernized life in the Canal Zone, and the other in the relatively isolated Bocas del Toro district in a subsistence economy. A third group, the descendants of Spanish slave laborers, live along the Atlantic Coast between Portobelo and Santa Isabel, also in a subsistence economy. The approach is to study incidence of a generally accepted risk factor, hypertension (which has a high incidence among Blacks in the U.S.), in a black population with fairly common hereditary but with differing environmental backgrounds extending back several generations. Valuable data from this study is expected within the next several years.

A long-term study of the natural history of cerebrovascular disease in Rochester, Minnesota, extending from 1945 through 1969, has shown a trend toward gradually increasing survival, and a gradual decrease in incidence rates. The investigators are reasonably certain that the decrease is not a reflection of changes in diagnosis, and feel that it reflects generally better treatment, including the increasing use of blood pressure lowering agents.

Outlook

There continue to be many urgent needs in the field of cerebrovascular disease. With increasing numbers of Americans moving into age groups at risk for stroke, continued research is important, both for stroke prevention and improvement in the quality of life for stroke victims.

THE EPILEPSIES

In a recently released report, the Epilepsy Foundation of America presents strong evidence that there are at least four million persons in the United States who have some form of epilepsy and that the total cost of their disabilities to the Nation is $4.25 billion a year. Less than ten percent of that, but still a very large amount ($325 million) is spent by the Federal Government for helping persons who have epilepsy through the many programs for aid, rehabilitation, benefits, medical assistance and veterans' care. Another $85 million is paid out by state and local governments for special educational requirements for those handicapped by seizure disorders. Only about one percent of these governmental expenditures ($4 million) is spent on the research effort to conquer the epilepsies.

Epilepsy is a symptom of several disorders of brain function manifested as brief episodes of unconsciousness, uncontrolled movements, erratic behavior or combinations of all three.

In about 60 percent of the known cases of the epilepsies, the symptoms, called seizures, are prevented by drugs, or in some instances, surgical treatment. In the other 40 percent, control of attacks is partial or is absent.

If attacks are controlled, a person with epilepsy can compete for a place in the world as well as a person who is not afflicted. However, when even as few as one or two very brief attacks a year occur without warning, employment and drivers' licenses are hard or impossible to obtain. When attacks occur often, it is difficult and often impossible for an afflicted person to exist without help. Obviously, total control of seizures is a very important goal.

To increase the percentage of completely controlled cases, to decrease unwanted side effects of some antiepilepsy drugs, and to try to find causes of and preventives for the epilepsies, the Department supports basic, clinical, pharmacological and surgical brain research, scientific comparisons of the effectiveness of existing antiepilepsy drugs, improved communications between researchers and public education. This research responsibility is centered in the National Institute of Neurological Diseases and Stroke of the National Institutes of Health.

Obligations for programs in the epilepsies

	1971	1972	1973	1974 estimate	1975 estimate
National Institutes of Health					
National Institute of Neurological Diseases and Stroke...	$3,194,000	$5,007,000	$4,035,000	$6,605,000	$6,449,000

NATIONAL INSTITUTES OF HEALTH

National Institute of Neurological Diseases and Stroke

The Disorders

Basically, man may be thought of as essentially a brain system (including nerve networks, and sensory organs) enclosed in and attached to a body which does physical work and provides the oxygen and nutrients the brain system's cells need to live and function.

The brain receives information both from the body and from the outside world through the sensory organs and nerve networks. It processes and stores that information and acts through nerves and muscles to move, communicate, and function internally as necessary. It also regulates consciousness and sleep, and by selecting from stored information decides directions and actions, and when, why, and how to accomplish its objectives.

As those brain processes take place, electrochemical-energy impulses sweep along the nervous system's cells (neurons). Whenever some neurons have a task to perform, they release bursts of energy to do the job, then turn off. The bursts are carried to their destination, the job is done and no more bursts arrive. Sometimes, in some persons, certain neurons or groups of neurons fire longer than needed for the task at hand. It is as if an electrical switch sticks "on" and power continues flowing longer than it is wanted; then the switch finally closes. Often other groups of neurons "turn on" too and additional electrochemical discharges go to many different and unintended places for the duration of the overflow. During the period of unwanted discharges, parts of the body controlled by the involved cells may perform erratically. When these episodes of uncontrolled discharges happen repeatedly, a person is said to have epilepsy. The erratic physical movements or alterations of consciousness are called "seizures."

Seizure discomfort and dysfunction range from mild to incapacitating and usually result in unconsciousness. Seizures may be simple partial where an eyelid flicks, a finger or a hand shakes, mild stomach discomfort is felt, a mouth corner jerks or the person speaks nonsense, is dizzy or experiences unusual or unpleasant sights, sounds, smells or tastes without loss of consciousness. They may be complex partial where the person experiences a dreamy state, either not moving or moving automatically but inappropriately for the time and place. Or there may be excessive emotions of fear, anger, elation or irritability, with no later recollection of them.

Seizures may be generalized when both brain hemispheres become involved and both sides of the body react causing eye blinking or upturning in the milder types (called absence seizures). Or, there can be complete body involvement with intense muscle rigidity followed by jerky alterations of muscle relaxation and contraction and severe stomach cramps in the more severe types (tonic-clonic) all with unconsciousness. Some seizures start as partial and progress to generalized as the original malfunctioning cells pick up support from other cells and uncontrolled discharges spread rapidly over the entire brain and out to the body.

Other seizures cause muscle flabbiness (atonic), muscle rigidity (tonic), muscle spasms (clonic), rythmic muscle jerks (myoclonic), or complete muscle collapse (akinetic).

Seizures may occur frequently or only occasionally, may last from a few seconds to several minutes and may be preceded by "auras" or warnings and followed by periods of confusion and exhaustion. In a severe form of epilepsy called "status epilepticus," seizures follow each other so closely that they appear to be continuous and can last for hours and may end in death if not stopped. Generally, unless a person who has epilepsy has other brain system damage or disabilities, intelligence falls within the same ranges as the general population and, when seizures are controlled, earning potentials are similar. Although it is now strongly suspected that frequent, untreated seizures may cause irreparable damage to neurons, and early diagnosis and treatment of seizures is being stressed, the fact that one has epilepsy does not mean that he or she is retarded or mentally ill.

Causes

The epilepsies are not contagious. There is some evidence that some types or susceptibility to certain types may be hereditary. More than half of the persons who have seizures are under twenty. Yet, it is possible for anyone at any age to become a victim, through brain injury.

Most researchers agree that brain damage has something to do with causing the epilepsies. They know that seizures often follow unusual birth trauma, severe drug or alcohol intoxication, head wounds, fever and some infectious diseases. They also are able to cause seizures in humans and experimental animals by surgical brain injuries or by certain chemical or electrical stimulation. Seizures are also associated with brain tumors, abscesses and congenital malformations. For many cases where no record of possible injuries exists, the term idiopathic (cause unknown) is applied.

Need for Research

Although seizures are probably as old as man, little could be done for those who had them until the middle of the last century. Since then, discovery and continuous refinement of antiepilepsy drugs have greatly improved the chances of persons afflicted by epilepsy to lead normal lives.

Public understanding of these disorders must improve so that those whose seizures are completely controlled, can be considered normal like diabetics who are controlled by insulin. People generally need to respect the rights of such persons, and of those whose seizures are not incapacitating, to equal educational, occupational, insurance and social opportunities. Treatments must be developed to improve the conditions of those more handicapped by their seizures so they too may lead independent lives. Scientists must learn enough about the human brain in health and dysfunction to eliminate the epilepsies. Research and early application of positive results are the only ways to bring this about.

Research Tools

The electroencephalograph (EEG), long used to study the epilepsies, uses electrodes on the scalp surface or microelectrodes in brain tissue to find and measure brain electrical activities. The EEG helps scientists to learn where an epileptic discharge begins, where it spreads, its intensity, duration and time of occurrence. It is the best diagnostic and research tool yet developed for seizure disorders.

Telemetering-computer equipment makes it possible to record and store a patient's EEG while he or she goes about normal activities. In telemetering, a patient wears a device which holds electrodes in place on the scalp and houses a small radio transmitter. EEG signals are picked up by a receiver and tape recorded. This provides greater accuracy than even trained observers in identifying and measuring seizures. Tape recorded seizure information can be reviewed repeatedly for research. Computers analyze experimental data and help to identify electrical patterns before, during, and after seizures. The latter capability is being used to develop seizure-warning devices. Also scientists are investigating the possible future use of computers to replace electroencephalographers in reading EEG's.

Animal models provide experimental-animal seizure cases similar to human cases on which drug and surgical treatments can be tried. They are created by altering brain or body physiology and chemistry and by electrical, chemical and sensory stimulations.

Drug therapy began in the 1850's with potassium bromide, progressed to phenobarbital by 1912, and was greatly improved with the introduction of diphenylhydantoin (Dilantin) in 1938. In 1946, trimethadione, the first effective treatment for absence seizures became available. Phenobarbital and Dilantin are still the best drugs for effective and safe use in controlling seizure activity. The ultimate physiological and biochemical actions of antiepileptic drugs is not known. Further research into the mechanism of actions of these drugs in seizures may well lead to a breakthrough into the cause of seizures.

Today there are 13 standard drugs marketed for epilepsy treatment in the United States. They are:

Trade name	Generic name in the U.S.	Year introduced
Luminal	phenobarbital	1912
Mebaral	mephobarbital	1935
Dilantin	diphenylhydantoin	1938
Tridione	trimethadione	1946
Mesantoin	mephenytoin	1947
Paradione	paramethadione	1949
Phenurone	phenacemide	1951
Gemonil	metharbital	1952
Milontin	phensuximide	1953
Mysoline	primidone	1954
Celontin	methsuximide	1957
Peganone	ethotoin	1957
Zarontin	ethosuximide	1960

Two hundred and fifty clinical studies purporting to show efficacy of various epilepsy drugs were reviewed recently. Only 110 included actual scientific trials and only three of those had been statistically tested. The other reported results had been based primarily on clinical judgment.

No new drugs for long-term use in epilepsy have been approved since 1960. This is due in part to 1962 changes in the laws which now require more stringent proof than formerly of efficacy and safety. In 1968, diazepam (Valium) was marketed as an adjunct drug for short-term use in status epilepticus. Research to date has not shown that this drug would also be effective when given on a continuing basis.

Gas-Liquid-Chromatography (GLC), long used to measure minute quantities of chemicals in solutions, is now routinely used to measure levels of anti-epilepsy drugs in patients' blood. With it, physicians can maintain therapeutic, nontoxic drug levels. It also provides proof as to whether or not a patient is taking the prescribed medicine. Researchers use it to compare drug effectiveness and to evaluate different patients' physiological responses to drugs. Many laboratories now provide GLC drug-level measurements although a large variation among laboratories indicates a need for biological standardizations.

Surgery is sometimes used as treatment in cases of complex partial seizures where medication does not control attacks, where attacks are frequent and incapacitating, and where surgery will not cause more seizure-generating damage or impair other functions. While most such procedures are routine now, data obtained before and after surgery are invaluable for better management of similar cases and for gaining further knowledge of abnormal brain function.

The Program

Basic Research (Extramural)

Five epilepsy research centers are supported by the Institute through three-to-five-year specialized clinical research center grants. They are at the University of California at Los Angeles, the University of Utah, the University of Washington, the University of Wisconsin and the Yale University School of Medicine. Each center concentrates on specific areas of research--basic brain research, antiepilepsy drug mechanisms, animal models, drug and surgical treatments of humans. These centers generate valuable knowledge about basic brain functions and continue developing useful new techniques for managing the epilepsies.

Additionally, there are over 100 NINDS-supported epilepsy-related projects in 14 states and five foreign countries. They are probing animal, human and non-biologic systems to provide better information in the areas of cause, diagnosis, and treatment. For the past seven years there has been increased emphasis on funding of projects which focus on treatment research.

Surgical Research (Intramural)

Relationships between overall pre-surgical and post-surgical patient factors are studied carefully and analyzed by the Institute. From brain surgery comes valuable observations of brain systems, advanced surgical techniques, better surgical devices, and better post-operative treatment regimens. Improved brain scanning in diagnosis, use of microscopic and stereotaxic equipment and increasingly precise charting of brain areas is making surgery more effective and safer. Surgical research also adds to knowledge of brain functions.

Perinatal Research (Collaborative)

Through a Collaborative Perinatal Research Project supported by NINDS since 1959, scientists at 14 medical centers have collected data on mothers and babies in 58,000 pregnancies--the largest prospective study of its kind ever undertaken. Most of the offspring are being followed through their eighth birthdays. The aim is to learn more about causes of numerous, serious neurological disorders, including those epilepsies that have their origins in events before birth and for several years afterwards.

More than 48,000 children completed their 12-month examinations by 1967. Analysis of the data gathered on them is just being published. By mid-1973 more than 40,000 of the children had received their seven-year examination and the project will end in mid-1974 when speech and hearing examinations at the eighth year will be complete on approximately half of the project's total of 40,000. Final data analyses in 1976 are expected to provide new clues on the epilepsies and their causes.

Drug Research Program (Collaborative)

The Institute's Collaborative and Field Research Program conducts and supports a considerable amount of the Nation's antiepilepsy-drug research efforts. That research is guided by an NIH Advisory Committee on the Epilepsies which comprises medical school, drug industry and Government representatives.

Free exchange of experimental information between drug companies and the Institute's programs enables the Advisory Committee to keep informed of progress and provides industry with expert advice before starting lengthy and expensive animal or human trials. Eight drug companies have provided information about their drugs. Four companies' drugs are undergoing evaluations through NINDS contracts.

At the University of Virginia and the Medical College of Georgia, a new experimental drug, clonazepam, is being compared with Zarontin in treatment of generalized absence epilepsy. At the New Castle State Hospital, New Castle, Indiana, combinations of Tegretol (approved for another disorder but experimental for epilepsy), phenobarbital and Dilantin were tested for effectiveness in controlling intractable generalized tonic-clonic seizures. Final results are due early in 1974.

A two-year University of Washington evaluation of the experimental drug sulthiame in comparison with Dilantin showed that sulthiame is not effective as single drug treatment for complex partial seizures. Researchers there are now embarked on an 18-month similar comparison between Tegretol and Dilantin. Also at the University of Washington, a study on primates is investigating relationships between blood drug-levels, seizure frequency and behavior changes. Others are probing drug effects on chemically or electrically induced seizures in animals which resemble the seizures experienced by humans.

Three recent Advisory Committee recommendations are being carried out and are at various stages of completion. One at the Lafayette Clinic, Detroit, studied the psychological and EEG correlates of Tegretol in complex partial epilepsy. The drug was found effective when added to regular treatment, but, contrary to some other reports, provided no psychological benefit. Lafayette Clinic scientists are now engaged in a similar study of combinations of Tegretol and Mysoline with the same population. The latter study is scheduled to end in 1974. Another recommended pilot study is at the University of Kansas Medical Center where investigators seek to learn whether immediately initiated and extended antiepileptic drug treatment for head-injury victims will decrease the number of post-traumatic epilepsy cases. The third is a completed study conducted by the Parke-Davis Company of how Dilantin is metabolized through multiple pathways by humans.

For the first time since efforts began for closer cooperation between the Institute and drug manufacturers, data from NINDS-sponsored studies (New Castle, Indiana, Universities of Virginia and Georgia) have been incorporated by companies in their New Drug Applications to the Food and Drug Administration. Additionally, the Institute is exploring cooperation with industry and the academic community.

The Institute's pharmacology laboratory personnel are studying how the brain receives, absorbs, metabolizes and excretes antiepilepsy drugs, how combinations with other drugs work and how to measure new experimental-drug levels in patients' sera. The laboratory also provides blood drug-level services to researchers conducting Institute-contract drug studies and offers guidance to other laboratories that provide drug-level measurements to scientists and physicians. The laboratory plans to monitor the development of reference standards for private laboratories to aid in quality control, now achieved by exchange of samples.

Finally, the Advisory Committee has recommended that the Institute develop a Comprehensive Epilepsy Program with objectives to: (1) support clinical and appropriate laboratory research in diagnosis, treatment, prognosis and prevention of epilepsy; (2) train and educate physicians and other professionals in new advances in epilepsy research and treatment and establish a broad public education program; and (3) demonstrate to those with epilepsy the value of up-to-date preventive, medical and rehabilitative, psychological, vocational, educational and social services. Objectives would be achieved by effectively coordinating epilepsy-related research, teaching and health-care delivery services in a given geographical area and by extending existing services to speed applied research. Such services would complement existing resources. The Institute is now evaluating proposals for feasibility studies on pilot projects of such Comprehensive Epilepsy Centers.

Research Progress

Causes

It has been said that no brain disorders have revealed more about the organization of the human brain than have the epilepsies. These disorders are unique among brain dysfunctions in providing neurologists many opportunities to examine the intimate neuronal mechanisms underlying a major health problem. At the same time, studies of seizure activities open valuable approaches to analysis of biochemical, genetic and environmental factors which contribute to brain processes.

Scientists have tried for some time to create in animals various kinds of brain damage and seizures similar to those which afflict humans. They have been relatively successful in applying several chemicals to the brains of animals and causing local reactions (foci) which later produce recurring seizures. They have also used electrical stimulation extensively but with limited success. The search for additional useful models continues.

Two researchers in Vancouver, B.C., have developed in cats "a condition strikingly similar to human epilepsy with spontaneous electrographic discharge and spontaneous epileptic seizures." They followed a technique called "kindling" which was pursued earlier by another Canadian in Ontario. The "kindling" phenomenon results when electrical stimulation at a constant intensity is applied to an animal's brain repeatedly over a period of a month or more. At first the stimulations cause no brain discharge. Later, brain discharges occur with stimulation until epilepsy-like spontaneous brain discharges trigger without further stimulation. The condition appears to be permanent once it is established. The seizures thus created are the first so far obtained by external factors which resemble the clonic-tonic type which used to be classed as "grand mal." The investigators suggest that injuries so produced, causing a usable, generalized, tonic-clonic-epilepsy animal model, are deep in the brainstem rather than in the forebrain as earlier believed.

Another new method for producing a convulsive disorder in animals--removal of the pineal gland after removing the parathyroid glands--was refined this year and studied further by a group in Texas. The technique was first developed in 1972 and has now been studied to identify the nature, frequency and time course of resultant seizures and to determine the effects of several drugs on seizure activity. Violent tonic-clonic convulsions occurred in rats when the parathyroids were removed first and followed a week later by pineal gland removal. But if either operation was done alone or the pineal gland was removed first, there were no convulsions.

Such seizures were delayed by phenobarbital, Valium or chlordiazepoxide, but were not affected by Dilantin, various pineal gland constituents or by calcium gluconate. All of the animals which developed seizures died within the succeeding 48 hours during seizures. Ultimate value of animal models is yet to be determined.

With animal models, neurochemists have learned much about brain structure and its chemistry. What they learn gives them opportunities to adapt antiepilepsy agents to treatment of human patients. Thus, over the past three years, investigators have determined that in human patients brain sites of maximum seizure activity show, among other things, low levels of an amino acid, taurine. Similar low levels of this substance are also noted in the seizure foci of cats rendered epileptic by applying the chemical cobalt to their brain surfaces. In the latter cases, the degree of abnormality in amino acid content coincides closely with severity of the seizures.

Recently, when scientists in Montreal injected taurine into mice and cats with cobalt-induced seizures, there was general abolition of convulsions in all instances within a period of hours. Abnormalities in amino acid content associated with the epileptic foci also disappeared. The observations suggest that taurine stimulates biochemical processes in the central nervous system which aid in recovering from cobalt-induced epilepsy. Conclusions were that taurine may serve as a powerful and safe antagonist of a type of epilepsy which closely resembles chronic, focal epilepsy in man. Also, that among amino acids, this action of taurine appears unique and warrants further investigation.

Since that report, limited clinical human trials with taurine have been inconclusive. Further trials are needed to establish whether or not taurine is effective in controlling siezures.

Pharmacologic Therapy

Within the past decade, pharmacologic information has accumulated rapidly for the most frequently used antiepileptic drugs. This information and the application of gas-liquid-chromatography to measure levels of drugs in patients' blood samples have made more effective use of drugs possible. Physicians can now be sure that the correct amount of drug is present within a patient's body, can prevent many toxic side effects, and can improve treatment results.

It is well known that without counseling 10 to 20 percent of patients fail to take their medicine regularly and often unfairly blame the drug for lack of successful seizure control. Further, epileptic patients often take other drugs for other conditions and those influence the levels of the antiepileptic drugs through interaction. Nearly half of all epilepsy patients take more than one antiepileptic drug regularly and when toxicity occurs, their physicians often are unable to determine which drug (or drugs) is causing the problem.

Research has shown that absorption of Dilantin varies more among patients than either phenobarbital or Mysoline does. Researchers in Toronto and in Florida found that Dilantin given intramuscularly is absorbed very slowly and may produce crystal deposition and local muscle irritation. Thus, if it is urgent to have control of seizures, intravenous doses of the drug should be given. Other researchers showed that steady-state blood levels from orally administered Dilantin are not reached for five to seven days. This information helps physicians decide whether to change dosage in that period. Other investigators found Dilantin given once or twice a day is as effective as when given three times a day, making it easier for patients to remember proper intake.

Available drugs still cause some undesirable side effects. Recent evidence suggested that antiepileptic drugs may increase the risk of congential malformations in infants of mothers who took these drugs during pregnancy. All such studies agree that populations studied so far are exceedingly small, and it is not justifiable to incriminate anticonvulsants as teratogenic agents.

The search for new drugs continues. In the earliest of several tests of Tegretol made for NINDS at New Castle, Indiana, a double-blind study was used in 45 institutionalized patients whose seizures were not completely controlled by combinations of antiseizure drugs in doses judged adequate by blood-level measurements. The object was to learn the effectiveness against seizures, the biological availability of the dose in the body and the degree of patient tolerance for the drug. In this 14-week study, Tegretol equaled Dilantin or phenobarbital in efficacy with minimal side effects. While transient episodes of low white blood cell counts (leukopenia) occurred, they were deemed of little importance. This and reports from other countries indicate that Tegretol is very promising.

Surgical Therapy

A recent, widely publicized treatment for epilepsy involves a surgically-implanted plate of silicon-coated, dacron mesh with four pairs of platinum-disc electrodes placed on the cerebellum--a structure at the lower rear of the brain--through which electrical stimulation is applied constantly. The New York neurosurgeon who developed the technique discussed eight patients who had received stimulation this way. Five were said to be markedly improved afterwards. Two others were considered somewhat improved. One attempt failed. This device and its implantation in humans followed directly from data obtained in experiments by NINDS-supported studies in animals on the role of the cerebellum in the control of seizures. Although there was guarded optimism at the results, epilepsy scientists expressed the need for more data: What degree of success can be realized in a larger group of patients? Can control be maintained over a long period? Will changes occur in the brain from the implanted electrodes and the constant stimulation, and if they do, will they be harmful or permanent? What happens if stimulation is turned off? Much attention will be given to this area of research in 1974.

Diagnosis

A Vermont neurologist, continuing work which first attracted attention four years ago, has suggested that marginal blood supply to the motor control areas of the brain caused by congenitally restricted distribution of blood vessels may contribute significantly to development of complex partial epilepsy in children. Earlier this investigator had discovered in some autopsied epilepsy cases abnormally small arteries in the part of the brain called the uncus and suggested that X-ray angiography which could show such arteries would be helpful in diagnosing idiopathic epilepsy cases. Drawings made recently of 52 normal brains studied after autopsy, showed that two percent of them had a scarcity of blood vessels leading to that important part of the brain which controls motor and premotor activity. This investigator hopes to stimulate interest in this aspect of epilepsy by calling attention to the variability of brain blood supply.

Epidemiology

An NINDS staff study was conducted in Washington County, Maryland, in an attempt to develop a method for counting children with epilepsy independent of treatment facilities. Results showed a prevalence rate on 18.6 per 1,000 population (two percent) for the 8-9-year-old children of the whole community and suggested that a questionnaire study can be effective in epidemiology studies. A method independent of treatment facilities was thought better for comparability between geographic regions than has been available previously. A questionnaire survey was used. Forty-two questions were posed about symptoms and signs of various types of seizures; 2,042 questionnaires were mailed to families of third grade children. Answers were received from 1,866 families. Later 200 of the children whose parents answered the questionnaire were given clinical examinations for epilepsy to check the reliability of the answers given. Applying other factors to balance the whole community, the researchers concluded that the questionnaire used could not discriminate between different forms of epilepsies, and that further evaulation of the questionnaire is needed.

Communications

Scientific Information Interchange

Research-generated knowledge is useful only to the degree that it is communicated to people who can use it. To aid scientists working on epilepsy, the Institute:

1. Published Epidemiology of the Epilepsies as Institute Monograph No. 14. It resulted from a conference on epidemiology in 1971.

2. Continued its contractual agreements with Excerpta Medica for monthly publication of Epilepsy Abstracts and its distribution to some 1,300 subscribers at a subscription rate of $20.50 per year.

3. Sent representatives to the 12th International Congress of Epilepsy in Barcelona, Spain, in September. Dr. J. Kiffin Penry, Chief of the Applied Neurological Research Branch of the Collaborative and Field Research Division was elected Secretary-General of the International League Against Epilepsy to serve until the next Congress in the Netherlands in 1977. The same representatives attended an international conference on drug interactions in Milan, Italy, just after the Barcelona Congress.

4. Sponsored a two-day Workshop on Neurosurgical Management of the Epilepsies in December at which the Nation's leading epilepsy neurosurgeons presented drafts of chapters proposed for a publication on this subject which may be ready in 1974.

5. Was represented at the December meeting of the American Epilepsy Society in New York City where Dr. J. Kiffin Penry was chosen president-elect of that organization.

Public Information

The Institute filled requests for 77,402 pamphlets, monographs, and magazine reprints on the epilepsies from the scientific, medical, paramedical, and lay public. The materials included Epilepsy, Hope through Research and Research Profiles 1972 for public inquiries; and for scientists monographs entitled Epidemiology of the Epilepsies; The Clinical Neurophysiology of Epilepsy--A Survey of Current Research; Epilepsy—A Review of Clinical and Basic Research; Studies on the Clinical Efficacy of Marketed Antiepileptic Drugs; a booklet Blood Level Determinations of Antiepileptic Drugs--Clinical Value and Methods; and a pamphlet of literature citations on Blood Level Determinations of Antiepileptic Drugs. Newspaper and magazine articles, health columns, radio and TV announcements and TV appearances by Institute scientists generated interest in the publications.

PARKINSON'S DISEASE

Parkinson's disease is a progressive neurological disorder affecting the brain centers responsible for control and regulation of movement. Estimates of prevalence range from one case per 1,000 to one case per 200 population. Most frequently attacking people in their fifties and sixties, parkinsonism is thought by some to be increasing in prevalence with the increase in average lifespan. The disease is rarely the primary cause of death, but it often weakens the victim so that he falls prey to other diseases. The National Institutes of Health has had a long standing responsibility for research and research support in parkinsonism, dating from the establishment of the National Institute of Neurological Diseases and Stroke in 1950.

Obligations for programs in Parkinson's disease

	1971	1972	1973	1974 estimate	1975 estimate
National Institutes of Health					
National Institute of Neurological Diseases and Stroke...	$3,302,000	$3,339,000	$3,342,000	$4,048,000	$3,610,000

NATIONAL INSTITUTES OF HEALTH

National Institute of Neurological Diseases and Stroke

Descriptions of maladies which were probably parkinsonism appear in ancient writings, but the first clear, detailed description was published in 1817 by James Parkinson, a London physician. As he noted, the three symptoms most often seen are tremor, rigidity, and a stooping posture. Lethargy, loss of facial expression, and difficulty in walking, talking, writing, or any action requiring a high degree of muscular coordination are also common. The intellect is ordinarily unimpaired.

Except for one form (postencephalitic) that appears to be the direct result of an attack of encephalitis, the cause or causes of Parkinson's disease are unknown. Certain forms may result from a still unidentified virus, and a few metallic poisons have been suspected. One theory on the cause is that coordinated muscle control depends upon a balance of two neurochemical systems, cholinergic and dopaminergic, and that the symptoms of parkinsonism are caused by overactivity or underactivity of one or the other of these systems. This theory has been strengthened by the fact that anticholinergic drugs such as Artane, which have been in use for many years, produce improvement in some cases whereas Reserpine, a tranquilizer known to antagonize dopamine, makes the symptoms worse. This theory has been further strengthened by work with dopamine.

Treatment

Treatment of parkinsonism in the past consisted of physical therapy to help counteract the muscular rigidity, brain surgery, now used infrequently and effective mainly against tremor, and drugs.

Recent research has shown that depletion of dopamine, one of the biogenic amine substances in the brain necessary for nerve transmission, accompanies parkinsonism. A researcher at Brookhaven National Laboratory, Upton, New York, now an NINDS grantee, in a series of highly successful experiments in the late 1960's found that it was possible to replace the missing dopamine by a gradual buildup of large oral doses of its metabolic precursor, an amino acid, levodihydroxyphenylalanine, abbreviated as L-Dopa or levodopa. This treatment benefited about three-fourths of all parkinsonism patients. Levodopa was widely acclaimed as the first truly successful antiparkinsonism drug, and the work opened up new hope for patients and research opportunities for scientists.

The new therapy, however, has not been without problems. Chief of these has been the side effects caused by the extremely large doses necessary to control parkinsonism symptoms. Levodopa is broken down very rapidly in the body, and large doses are necessary to achieve the saturation required for penetration into the brain. A way around the problem has been found through the use of enzyme inhibitors, substances which slow the metabolic breakdown of levodopa, allow more time for it to penetrate, and make possible a reduction of dosages by as much as 80 percent. One enzyme inhibitor, labeled MK-486, has been undergoing trials at NIH and in a number of other institutions, and is expected to be ready for submission for approval by the Food and Drug Administration by October 1974.

The Research Program

The NINDS program in parkinsonism consists of grant support for several large interdisciplinary research groups, and 20 smaller, more circumscribed research projects.

One of the larger teams, headed by Dr. Robert Katzman at the Albert Einstein College of Medicine in New York, has embarked upon an ambitious and highly promising study of the whole group of neurotransmitter substances known as biogenic amines. (Dopamine and levodopa, mentioned above, are among such amines).

In one project, an instrument known as a cytospectrofluorometer is being used to determine precisely the location, distribution, and projections of amine-containing cells in the primate brain, as well as the type of amine contained within single cells. Super-thin slices of brain tissue containing amines which have been rendered fluorescent are examined, and the location of the cells plotted on a photograph of an adjacent stained section. This makes possible the tracing of nerve fibers from one region to another, and observation of changes in the fibers following surgical interruption of a particular amine pathway. The studies are being carried out in the cebus monkey, and will be extended to human brains obtained shortly after death. Although the project is of special interest to parkinsonism research, the scientists note that these widely spread aminergic neurons may also be the key to understanding many disease processes.

The biochemical systems in which neurotransmitters are formed, regulated, put to use, and finally disposed of are extremely complex and, at this stage, many details are only guessed at. Cyclic AMP, a regulatory substance active at and near nerve terminals, together with several related enzymes, is under special scrutiny at the New York center. The approach is to identify, and measure these substances in animal brains, then interrupt the nerve pathways in which they move and observe changes. The work is of potential importance in parkinsonism, which appears to be essentially an alteration or imbalance in the regulatory mechanism governing coordinated movement.

Other projects at the center study the relationship of the blood-brain barrier to the movement of amines, the behavioral effects of experimentally altered amine systems, and possible regenerative processes in aminergic systems in several animals (cats, monkeys, and rats).

At Brookhaven National Laboratory, Dr. George Cotzias, the scientist primarily credited with the development of L-Dopa therapy, heads an extensive biochemical and genetic exploration of parkinsonism, built largely upon his earlier work. First interested in manganese poisoning, the symptoms of which are similar to those of parkinsonism, Dr. Cotzias and his group continue to search for a role for manganese in neurotransmission.

By feeding manganese to newborn mice, they found that cerebral dopamine levels correspond almost exactly with cerebral manganese, and feel that this provides strong evidence that the metal may participate in the development of the dopamine neurochemical system, as well as in its normal functioning. As with some other trace metals, minute amounts may be necessary to life, but larger amounts may damage or destroy it.

In continuation of work reported last year with apomorphine, which appears to reinforce the effect of L-Dopa, the scientists studied a similar, possibly better drug, N-propyl-norapomorphine. It is more potent than apomorphine, and appears to be somewhat safer. The researchers also hope that it will lessen one of the most striking side effects of L-Dopa, the involuntary "twitching," movements.

Another possible adjunctive drug which the Brookhaven scientists are planning to try with L-Dopa is piperidine, a tranquilizer, which they hope will help patients displaying mental changes and irregular or involuntary movements, both common L-Dopa side effects.

Since L-Dopa therapy on a large scale is relatively new, its long-term side effects are still in question. Increased frequency of twitching movements, and mental and behavioral disturbances, noted above, have been widely experienced, and are the subject of intensive efforts to achieve pharmacologic control. Another long-term side effect--start hesitation--now seems to be increasing. This is described as a sudden episode during which the patient may experience a sensation of extreme heaviness of both feet and find himself unable to start walking. If unrecognized, frequent falls, with serious injuries may result. Institute grantees at Yale University, in a study of 51 patients on long-term L-Dopa therapy, found that six (or 12 percent) developed start hesitation. A slight reduction in dosage cleared up the problem in five of the six, with the sixth patient experiencing some improvement, but also a return of some of the Parkinson symptoms. Their conclusions were that start hesitation can be controlled and that it definitely does not indicate progression of the disease or drug tolerance.

A number of items of new statistical and genetic information were reported during the year. In one report, reviewing experience with 100 patients treated at the University of Minnesota, Institute grantees uncovered a distinct difference between theirs and previous similar studies. They were unable to relate a single case to a previous attack of encephalitis. (For many years physicians have diagnosed a specific form of parkinsonism as post-encephalitic, and assumed that the parkinsonism was a long-delayed after-effect of a world-wide encephalitis pandemic occurring in the period from 1916 through 1926.) Their findings clearly strengthen the view that the post-encephalitic form of the disease is declining in prevalence.

The researchers also found that 29 percent of their patients had relatives with Parkinson's disease, a higher proportion than has been found in most previous analyses.

In another study at the same institution, scientists estimated that for siblings of patients the risk of developing parkinsonism by age 75 was approximately 30 percent. While they note the likelihood of other causes, they presented strong evidence for a genetic pattern in possibly a majority of cases, and suggested the possibility that genetic mechanisms may regulate brain tissue levels of tyrosine hydroxylase, an enzyme critical to dopamine metabolism.

A form of parkinsonism, parkinsonism-dementia, or PD, occurs among the Chamorro speaking people of Guam and the other Mariana Islands at a far greater incidence rate than that of parkinsonism elsewhere in the world. It accounts for 10 percent of adult Chamorro deaths, and is rapidly progressive, leading to death in four to five years.

In an attempt to learn why PD is so devastating within this small, isolated population, the Institute's Epidemiology Branch operates a research center on Guam with a permanent staff, where patients are treated and studied. The search is focused on discovering possible genetic or familial factors, and also on uncovering any possible viral or toxic metal causes. Treatment of these patients with L-Dopa plus MK-486 has been highly successful in alleviating the Parkinson symptoms, although the dementia of PD has not been alleviated.

The patients have formed an important resource population for basic studies by NIH scientists of disturbances in amine metabolism, including the action of the enzyme tyrosine hydroxylase, and assays of spinal fluid. The Guam research center also serves as the setting for cooperative studies which bring in scientists from universities and other research institutions.

Outlook

Although great advances have been made in treatment of symptoms, the causes and methods of prevention and cure of Parkinson's disease are still unknown. However, research is helping to understand the disease and it is hoped will reveal clues to its cause and prevention. Gains made thus far, together with expected developments in the near future, have justified an optimistic attitude among scientists, physicians, and patients that control of this disabling disease can be achieved.

April 1974

NATIONAL INSTITUTES OF HEALTH

National Institute of Neurological Diseases and Stroke

HUNTINGTON'S DISEASE

The Problem

Huntington's disease is an hereditary disorder characterized by a combination of physical and mental symptoms, either of which may appear before the other. Often, however, the physical symptoms come first, and usually between the ages of 35 and 40, by which time the individual may have passed the disorder on to several children.

Early symptoms may be confused with fidgety nervousness. The uncontrollable chorea may show itself as abnormal involuntary movements, such as jerking, twisting, and spasms of the muscles of the face, tongue, neck, trunk, arms, and legs. As symptoms become more severe the patient may have trouble swallowing and may be unable to speak.

Huntington's disease also may begin with distressing personality changes, such as indifference, dullness, irritability, poor judgment, loss of memory, and carelessness about personal looks and habits. Outbursts of violence may occur, alternating with periods of short-lived depression. In later stages the patient may become profoundly demented.

Huntington's disease is passed on through an autosomal dominant gene, which means that each offspring of an affected person has a 50 percent risk of having the disease. Males and females and all ethnic groups may be affected.

If a person does not show symptoms by age 35, the probability of his having the disease diminishes with each succeeding year. In very rare instances, however, individuals over 70 years old have been known to develop the Huntington's disease symptoms.

Prevalence

Because of its hereditary nature and categorization as a "mental" disease, families have hidden its existence for centuries and it is almost impossible to assess accurately statistics regarding the prevalence of Huntington's disease in the United States.

A review of a number of studies on the prevalence of Huntington's disease in various world populations indicates a fairly uniform distribution which would mean that about 10,000 to 14,000 Americans have Huntington's disease symptoms. However, since the establishment of the Committee to Combat Huntington's Disease (CCHD), incoming letters, phone calls, and personal contacts have led the CCHD to believe that three to four times this number may have the Huntington's disease gene and either have Huntington's disease symptoms or will eventually develop symptoms.

Diagnosis

There is, as yet, no means to test and identify persons with Huntington's disease before symptoms become apparent. The diagnosis of Huntington's disease is usually based on the clinical findings of dementia, and chorea, and positive family history. The insidious onset of involuntary movements is unlike most other forms of chorea and can aid in the identification of the disease.

Early Detection

Early detection of Huntington's disease may be helped by knowledge of the family history and the expected age of onset from that in older siblings. Investigators report that the mothers of some large choreic families may be able to sense which children will develop the disease, and later events prove them to be correct.

Advances in Diagnosis

Preliminary findings from several federally-supported laboratories have sparked the hope that a test for the early detection of Huntington's disease is near.

In one collaborative study investigators have described a predictive test based on the observation that the drug levodopa aggravates choreiform movements in patients with Huntington's disease and might bring out undetected chorea in asymptomatic victims. When the effects of oral levodopa were compared in offsprings of choreics and controls, the children of choreics developed facial twitches and involuntary movements while controls remained unaffected. It has not yet been proven that individuals developing chorea with this test will develop the disease later, nor that those in whom the test is negative may not develop it in time. The National Institutes of Health is presently supporting research to investigate the effectiveness of such a test. If this predictive test proves reliable, it should be of considerable value in eliminating the disease. Attempts are now being made to refine the L-dopa test to find biochemical changes that occur without concomitant physical symptoms.

Other preliminary reports indicate that it may eventually be possible to detect Huntington's disease using less drastic approaches. National Institute of Neurological Diseases and Stroke (NINDS) grantee scientists in California have found that a certain type of cell (fibroblasts) taken from patients with Huntington's disease and cultured in the laboratory do not survive as long as cells from normal individuals cultured under the same conditions. This difference in cell life span may be useful in identifying Huntington's disease very early in presymptomatic victims. It is also hoped that such a test, if successfully developed, could be extended to intrauterine tests to detect Huntington's disease in the fetus.

While the development of a test to identify carriers before symptoms occurred would, of course, be of considerable value in genetic counseling, the question has been raised by a recent NINDS survey whether individuals who risk developing the disease would choose to know if they carry the defective gene. In the study 23 percent of the high-risk respondents--those under age 45 with a Huntington's disease parent—indicated that they might refuse to take a simple and safe predictive screening test if one is developed.

Cause

Until now the nature of Huntington's disease has been poorly understood. However, a recent report from a group of Canadian researchers may change this status. They found that the brains of patients who had died of Huntington's disease were deficient in a compound called gamma-aminobutyric acid or GABA. It is believed that GABA inhibits neural transmission in the brain and that a deficiency might produce the symptoms characteristic of Huntington's disease.

Support for this hypothesis recently came from a group of English scientists who reported a reduction in the activity of an enzyme (GAD or glutamic-acid-decarboxylase) in the brains of Huntington's disease victims. The reduced activity of this enzyme which is involved in the production of GABA indicates that certain GABA-containing nerve cells in the brain are malfunctioning.

Treatment

It is hoped that these exciting leads into the biochemical nature of Huntington's disease will pave the way for the development of a successful treatment. Until now the treatment for Huntington's disease was directed toward improving the involuntary movements of the patients. Presently a number of laboratories are directing their studies toward the evaluation of GABA as a therapeutic agent and correction of what appears to be the basic biochemical abnormality of Huntington's disease.

In one promising pilot study, two of seven Huntington's disease patients given large doses of GABA have shown striking improvement, one patient has shown moderate improvement, and the remaining four have remained unchanged.

At the National Institute of Mental Health, scientists have synthesized a compound similar to GABA but which may pass through the blood-brain barrier and enter the brain more readily than GABA. It is hoped that this agent will help "correct" the GABA deficiency and improve the patients' condition.

Research

The Department is presently supporting several types of research through the National Institutes of Health and the National Institute of Mental Health of the Alcohol, Drug Abuse, and Mental Health Administration, aimed at finding the cause, cure, and treatment of Huntington's disease and at disseminating information materials relating to it.

The NINDS funds seven regular research grants, a portion of a Program Project ~~and Categorical Clinical Research Centers~~ and two collaborative studies at $416,000.

Other research studies relating directly to Huntington's disease include six General Clinical Research Centers, funded by the Division of Research Resources at $78,787, and a portion of two Program Projects and Categorical Clinical Research Centers funded by the National Institute of Arthritis, Metabolism, and Digestive Diseases, and by the National Institute of Child Health and Human Development at $35,000.

In addition to these programs relating directly to Huntington's disease, the NINDS has an extensive program of basic research funded at $13,475,000 which is important in understanding the nervous system and the disorders which interrupt its normal functioning.

The Institute works closely with the Committee to Combat Huntington's Disease (CCHD), a voluntary health organization that encourages research in Huntington's disease. The CCHD plays a vital role in disseminating information about the disease and in providing psychological support for members of families affected with Huntington's disease. The Institute also has prepared a pamphlet for the public describing Huntington's disease and outlining current research which gives hope for the future. In writing the pamphlet, NINDS worked closely with CCHD.

April 1974

NATIONAL INSTITUTES OF HEALTH

National Institute of Neurological Diseases and Stroke

MENIERE'S DISEASE

Meniere's disease is a disorder of the inner ear (which contains the organ for hearing and for balance) characterized by the episodic occurrence of a triad of symptoms--vertigo (dizziness), transient hearing loss and tinnitus (ringing in the ears).

Although it can occur at any age, it appears most commonly in persons in the forties and fifties, somewhat more frequently in men than in women. Meniere's disease can be primary, occurring in persons without a previous ear disorder, or secondary, superimposed or as a consequence of some other disorder. In some patients, particularly those whose Meniere's symptoms can be attributed to a definite cause, drugs or surgery may be effective. However, in many patients, particularly those whose Meniere's disease is of unknown origin, the symptoms may become so severe that the patient is unable to continue working or completing everyday tasks.

The duration of Meniere's attacks are highly variable, occurring anywhere from twice a month to twice a year, and lasting from twenty minutes to twenty-four hours. In addition to the severe agony of vertigo, tinnitis and hearing loss during an attack, the patient may also experience nausea, vomiting and nystagmus (uncontrolled to and fro movements of the eyes).

Meniere's is a prolonged disease which gradually abates as deafness increases. Attacks may spontaneously disappear, or they may continually recur for years.

Research

The National Institute of Neurological Diseases and Stroke (NINDS) is supporting basic research to determine the causes of Meniere's disease leading to its prevention. Until Meniere's can be prevented, the Institute is also continuing to support research on improved methods of medical and surgical treatment to relieve symptoms.

Research has indicated that the underlying cause of Meniere's disease is an abnormal build-up of fluid (endolymph) in a part of the inner ear (labyrinth) known as the endolymphatic sac. Results of laboratory experiments using thorium, a radioactive tracer, show that it is likely that cell debris from damaged or dying cells is part of the normal cell turnover. However, these cells are not enveloped and consumed in the inner ear by special cells, known as phagocytes. Rather, they are transported to the inner structure known as the endolymphatic sac for excretion. If this sac is malfunctioning, the cell debris accumulates into groups (macromolecules) that are too large to be diffused (passed out of the sac through its membrane). This causes an increased osmotic pressure in the sac (more fluid passes into the sac than flows out of it), so that the sac's membrane becomes distended. This distension, or possible rupture of the membrane allowing fluid to flow out, interferes with two other inner ear structures, the cochlea (organ of hearing) and the vestibule (concerned with balance and equilibrium).

Meniere's disease therefore falls into two general types--cochlear or vestibular--depending on which of these two structures is primarily disturbed. As can be expected, the main problem for patients with cochlear Meniere's disease will be hearing, while the predominate problem for those with vestibular Meniere's disease will be balance.

Several factors, according to researchers, may be responsible for this abnormal build-up of fluid. Some of these factors, particularly in patients with secondary Meniere's disease, result from other disorders. For instance, clinicians in Los Angeles conducted a two-and-a-half-year study of 120 patients with Meniere's symptoms. They found a specific cause in 36 percent. These were: allergy, primarily to foods, responsible in 14 percent; malfunction of two glands, the adrenal and pituitary in six percent; acquired syphilis in seven percent; hypothyroidism in three percent; narrowing of the auditory canal (compressing its contents) in three percent; and trauma (from noise or physical damage) in three percent.

Researchers in Missouri and Tennessee have reported an apparent association between inner ear dysfunction and diabetes. A St. Louis clinician found 19 patients with Meniere's symptoms had previously undiagnosed diabetes, and has proposed mechanisms by which diabetes might produce lack of oxygen to the inner ear.

Treatment

In instances where a specific cause of Meniere's symptoms can be found, appropriate drugs may be effective. In fact, it is estimated that approximately 80 percent of persons with Meniere's symptoms can be helped to some degree in this way. For instance a Chicago clinician who is an associate in otolaryngology at Northwestern University Medical School, recently reported treating several hundred patients whose Meniere's symptoms were apparently caused by food allergies by regulating diet (including alcohol and tobacco). Meniere's symptoms arising from other allergies are sometimes helped with histamines. Meniere's symptoms due to malfunction of the adrenal or pituitary glands can often be alleviated with hormone replacement therapy; symptoms due to hypothyroidism can be helped with thyroid replacement therapy; vasodilators (which expand arteries to increase blood flow and therefore oxygen to the inner ear) relieve symptoms resulting from a narrowing of the auditory canal; and the steroid prednisone may help reduce the severity of Meniere's symptoms resulting from syphilis infection.

For persons with Meniere's disease of unknown origin, however, the situation is more bleak. Psychotherapeutic drugs, such as Valium, often help aleviate vertigo which is usually the most devastating symptom. But these drugs do not cure the disease or arrest its occurrence. At the present time, there are no drugs which can alleviate the symptoms of tinnitus, although scientists are continuing the search.

Recently there has been a resurgence of interest in exploring the use of streptomycin in the middle ear to combat Meniere's disease. Scientists have known for some time that streptomycin destroys vestibular function. Animal studies by scientists at Northwestern University indicate that streptomycin may selectively destroy the vestibular (balance) system leaving the cochlear (hearing) system intact. Their studies also indicate that streptomycin may improve the balance of sodium and potassium, (responsible for maintaining osmotic pressure in the endolymphatic sac) which goes awry in Meniere's disease. When only one ear is involved, the scientists use streptomycin topically in the middle ear, while in younger patients with both ears involved, they inject the drug.

Surgery is becoming increasingly safe and effective in combatting Meniere's disease and is becoming a viable alternative in patients who cannot be adequately helped by drugs. There are three types of surgery: decompression (drainage) of the endolymphatic sac to re-establish normal inner fluid pressures; severing (denervating) inner ear nerves; or destruction of the inner ear structures when hearing is already extremely poor.

Decompression surgery is most often accomplished using a "shunt" which connects the endolymphatic sac fluid space to the subarachnoid space (the space just outside the spongelike membrane which covers the brain and contains spinal fluid) so that the pressures of these two systems remain equal. This surgery is often beneficial in patients with both ears affected who have retained useful hearing.

Severing inner ear (labyrinthine) nerves has been found to be most effective in patients who have retained good hearing but have constant unsteadiness. Although the operation is effective against dizziness, it has no effect on preventing further hearing loss.

Destruction of the inner ear is used only for patients with very poor hearing who do not respond to other measures and seek relief from dizziness. New surgical methods, ultrasound and cryosurgery (freezing) are sometimes being used for this operation.

NINDS-supported scientists at the University of Washington, St. Louis, have followed 20 surgical Meniere's patients for six months. They report that remission periods (attack-free) in the patients have lasted 10 times longer than those prior to surgery. They also report that hearing improved significantly in 56 percent of the patients; 25 percent experienced some hearing improvement; while 20 percent had no improvement. Improved diagnostic procedures including polytomography (a type of moving X ray), medical history, and methods for detecting fluid build-up in the endolymphatic sac are helping these scientists develop a criteria for determining persons who will benefit from surgery. Their studies indicate that surgery may be helpful in one in every ten persons with Meniere's disease.

Outlook for Future

Recent advances in electron microscopy have enabled basic research scientists to gain a better understanding of the physiological basis of

Meniere's disease. While Meniere's symptoms produced by secondary causes now can often be cured, symptoms of Meniere's disease of unknown origin have been much more difficult to treat. Scientists at all levels are continuing to explore the possible methods of preventing Meniere's disease, and of curing it either medically or surgically so that its victims may be restored to a normal life.

SPINAL CORD INJURY AND HEAD INJURY

Spinal cord injury can result in paraplegia, quadriplegia, or partial paralysis. In terms of human suffering and economic loss, severe injury to the spinal cord is the most devastating of all personal tragedies because once destruction to the spinal cord has occurred, nothing now known can reverse the effects of the injury.

The National Paraplegia Foundation, a national voluntary health agency, estimates that there are 125,000 paraplegic and quadriplegic patients in the United States today. Insurance figures indicate that there are 10,000 to 12,000 new civilian paraplegics each year. Four out of five victims are males between the ages of 15 and 25 who are injured in vehicle, sporting or industrial accidents or as a result of gunshot wounds or falls. Because of their youth at the time of injury, many victims face as much as a half century in bed or wheelchair, without conscious sensation from the waist down.

The cost of initial hospitalization and lifetime care of the spinal cord injured plus indirect costs in terms of lost earning capacity for the individual and reduced productivity for the Nation total billions of dollars each year.

Three million Americans sustain injuries to the head annually; 50,000 die from trauma to the brain, the majority being caused by traffic accidents. An estimated 250,000 citizens are permanently disabled each year. In contrast to stroke, mortality and morbidity rates from head injury are lower, but affect a younger population--students, wage earners, homemakers. The life expectancy for disabled survivors is therefore many years longer, and the economic cost to the Nation has been estimated by the National Institute of Neurological Diseases and Stroke (NINDS) at $1.5 billion annually.

The Department of Health, Education, and Welfare's responsibilities for programs in Spinal Cord Injury and Head Injury are centered in the National Institute of Neurological Diseases and Stroke of the National Institutes of Health for research, and in Maternal and Child Health of the Health Services Administration for service.

Obligations for programs in spinal cord injury and head injury

	1971	1972	1973	1974 estimate	1975 estimate
National Institutes of Health:					
National Institute of Neurological Diseases and Stroke..	$3,578,000	$4,665,000	$5,613,000	$8,460,000	$8,386,000
Health Services Administration:					
Maternal and Child Health........	[1]	[1]	[1]	[1]	[1]
Total...............	3,578,000	4,665,000	5,613,000	8,460,000	8,386,000

[1] Obligations not identifiable.

NATIONAL INSTITUTES OF HEALTH

National Institute of Neurological Diseases and Stroke

SPINAL CORD INJURY AND HEAD INJURY

Spinal Cord Injury

The spinal column or backbone is composed of a stack of 33 circular blocklike bones, called vertebrae. A single vertebra is a flat, roughly circular bone with rearward-projecting knobs to which muscles are attached. There is a hole or canal through each vertebra which provides a protective bony channel surrounding the cable-like bundle of nerve fibers and cells which comprise the spinal cord. The cord carries fibers descending from the brain that innervate muscles and other bodily organs and also carries fibers ascending to the brain that send in sensations and other inputs from the body to brain centers.

Causes of Spinal Cord Injury

Injury to the nerve roots or substance of the spinal cord may occur directly from falls on the back, as from heights; industrial accidents; jumping to escape from fires; stab wounds, gun shot, shrapnel, and other penetrating missiles; birth trauma, especially breech presentation; and fracture or fracture dislocation of the vertebral bodies. It should be emphasized, however, that the latter is of little practical importance except when injury to the bony spine affects the spinal cord or its roots. For example, a person can have a "broken back" without a spinal cord injury.

More frequently, however, injury to the spinal cord occurs indirectly as from excessive flexion or extension of the spine in falls, diving, and automobile accidents. Thus, if a motor car is struck from behind, the passenger's head is whipped back. If the vehicle stops abruptly, he may be jackknifed forward. Sometimes a sudden fall may cause the head to strike in a position that flexes the neck acutely, e.g., football injury or slipping on an icy pavement. Hyperflexion of the spine is the most common mechanism of spinal cord injury and is occasionally produced without external force during spontaneous or induced convulsive seizure.

Disease as well as trauma can injure the spinal cord and result in paraplegia. These diseases include cancer and other tumors of the spinal cord, infections and abscesses of the spinal cord, multiple sclerosis, congenital defects including severe forms of spina bifida, and other more rare neurological disorders.

Types of Spinal Cord Injury

Damage to the cord from trauma may follow: (1) simple concussion without direct trauma to the cord; (2) compression, contusion, or laceration of the cord substance by penetrating missiles or by fracture dislocation; (3) hemorrhage into its substance; and (4) compression of its vascular supply. Any level of the spinal column may be injured but in civil life the most common sites of injury are at the level of the fifth and sixth cervical vertebrae (vertebrae of the neck) and the eleventh and twelfth thoracic vertebrae (vertebrae of the chest and ribs).

Severity of Spinal Cord Injury

The severity of spinal cord injury depends upon the level of injury of the cord, not the level of bone injury. The central part of the spinal cord is soft and easily bruised and squeezed by pressure from surrounding bones. Thus cord damage can and does occur above or below the level of bone injury. The lower the injury on the spinal cord, the better off the patient is for the simple reason that more of the cord remains intact. Muscles controlled by nerves in the spinal cord above the injury often regain full function after the period of "shock" to the nerves wears off.

Conversely, injury in the upper cervical cord threatens life itself because of the development of respiratory paralysis. Fatalities in patients with lesions below the fifth cervical vertebra are uncommon in the period immediately following the injury in the absence of damage to other organs. Death may follow after a period of weeks or months as a result of bed sores, or bladder dysfunction.

The amount of cord injury is another key factor in determining severity and possible degree of recovery. Complete cuts of the cord, as from a bullet or missile fragment, cannot be repaired. Motor paralysis and sensory loss in these cases are permanent.

In the patients who survive spinal cord injury, some degree of improvement in the neurological signs is to be expected in all cases except where the cord is transected. The outlook is even better when the symptoms are due mainly to hemorrhage into the cord. As long as some nerve fibers in the spinal cord are uninjured, improvement in the patient may occur, usually during the first six months, but sometimes even longer after injury.

Management of Spinal Cord Injury

Since World War II, great progress has been made in the management of the patient with spinal cord injury. With the advent of sulfonamides and antibiotics, rapid transportation, and better rehabilitation methods, the entire philosophy for the care of patients with injuries to the spinal cord was revolutionized. An earlier despairing attitude has given way to hope of restoring the patient to his optimum state, not mere survival as a 24-hour-per-day bed patient. More recently, improved mechanical aids to ambulation, including a very new inflatable brace, special devices for operating an automobile, and public interest in removing architectural barriers to mobility, have offered limited participation in the mainstream of society to the spinal cord injured. Most important of all, there is now the first glimmering of hope that in some cases where the cord is severely injured--but not severed--function may be preserved. An even longer range possibility is that the old dream of regeneration of fibers in an injured spinal cord may be realized. This, of course, is the big hope of those already suffering from paraplegia.

Spinal Cord Injury Research Program

In its search for ways to deal effectively with the problem of paraplegia, the National Institute of Neurological Diseases and Stroke has developed approaches to four major areas of concern: treatment of acute spinal cord injury when the cord is not completely severed; regeneration of the spinal cord; development of an electrical "by pass" of the injured cord and a neural prosthesis for the control of urinary bladder action; and the use of angiography in the prognostic assessment and management of spinal cord injury.

New Approaches to Acute Injury

Conventional thinking about spinal cord injury has been that spinal function is immediately and permanently lost following traumatic disruption of the cord.

However, many years of laboratory studies with experimental spinal cord trauma conducted and supported by the NINDS and by universities and medical centers throughout the world now suggest that even severe physical injury does not always destroy the spinal cord. In some cases it has become evident that all of the tissue damage may not be directly related to the trauma, but may be an indirect result of it. Today, many scientists believe that the injury initiates a process of necrosis that eventually does destroy the cord. Within a definite time lag before this process is fully developed, the long fiber pathways are mostly intact. This raises the possibility that if this response of the tissue to injury could be stopped in the acute stage, then useful spinal cord function could be preserved and paralysis prevented.

To take advantage of these developments and to stimulate increased related research, the NINDS has established a targeted program on acute spinal cord injury. Through its extramural programs, the Institute is supporting five Acute Spinal Cord Injury Clinical Research Centers at: Ohio State University, Columbus; Yale University, New Haven, Connecticut; St. Joseph's Hospital and Medical Center, Phoenix, Arizona; The Medical University of South Carolina at Charleston; and New York University, New York City; and a large program project at the University of North Carolina at Chapel Hill where multidisciplinary basic research on acute spinal cord injury is being pursued. Additionally, there are three other targeted research programs on acute spinal cord injury at Washington University, St. Louis, Missouri; Hahnemann Medical College and Hospital in Philadelphia, Pennsylvania and the University of North Carolina at Chapel Hill.

It is generally acknowledged by scientists working in this area that new treatment of spinal cord injury must be based on new knowledge of the anatomic, physiologic, and biochemical changes that result from injury and that this knowledge must be applied before tha changes become irreversible.

Thus the aim is to develop techniques which will preserve or restore adequate circulation and provide metabolic support for the traumatized area to avoid secondary damage from inadequate nutrition.

Generally, scientists within the Institute's targeted research programs are studying pharmacologic agents, local cooling, surgery, steroids, and other modalities in a search for therapy that will preserve or restore spinal cord function.

Their goal is to establish a capability for assessing the effect of these agents or procedures designed to combat acute events leading to complete experimental transection of the spinal cord and, when safe to do so, applying them to patients.

Within its targeted programs on spinal cord injury, as well as through the regular research grants program, the NINDS supports a wide range of studies at the molecular and cellular levels. These investigations are directed toward clarifying processes responsible for enduring reflex and sensory alterations—spinal shock, hyperreflexia, pathological pain, and altered sensation. The overall goal of the studies is to provide a better foundation from which new therapeutic approaches to conditions arising from injuries to spinal roots and cord might evolve.

With the hope of promoting a useful exchange of information which is expected to come out of the Acute Spinal Cord Injury Research Centers, the Institute recently initiated a series of workshops. At the first of these, in March 1974, a primary goal was to correlate and standardize the experimental model of spinal cord injury. Also discussed were the most efficient ways to collect, store, and retrieve with analysis the data accumulated from experimental spinal injury studies and from human patients.

Valuable patient data will also be available from the National Spinal Cord Injury Registry established by the Defense Department in 1972. Nine hundred neurosurgeons in the U.S. and Canada are cooperating in this effort by sending the Registry a two-page protocol summary on patients under their care.

Nerve Growth and Regeneration

Restoration of function in paraplegia is one of the Nation's greatest medical challenges. It is also an extraordinarily difficult problem because it involves both regenerating interrupted spinal cord fibers and growing them to their original termination.

Progress in this area of research has now reached the point where scientists know that two kinds of regeneration occur following injury to the central nervous system: (1) terminal regeneration, in which an injured nerve simple regrows its severed nerve process and (2) collateral regeneration, in which normal intact nerve fibers in the region of denervated nerve cells sprout additional outgrowths which reinnervate the adjacent denervated cells and thereby function in place of the lost neurons.

These discoveries in the central nervous system regeneration and the quarter century of careful research which preceded them can contribute to potential breakthroughs in the field of paraplegic research. Their major importance is that they permit re-examination of the long standing belief that the central nervous system is incapable of regeneration and clarify the direction that future research must take.

As a result of these research advances and in response to the hope that regeneration in the nervous system may be possible, the NINDS has established a Section on Neuronal Development and Regeneration within its intramural laboratories. Also, an ad hoc subcommittee of the National Advisory Neurological Diseases and Stroke Council has been named to assess the current status of research on regeneration. Through its extramural programs the NINDS supports a large program project at New York University and a number of small research studies dealing with key questions such as how nerve cells grow, how they make such fantastically intricate connections, and what stimulates them to regenerate when injured.

It must be emphasized that the nerve growth and regeneration studies are all long-range projects that are presently in the early stages of development.

Neural Prosthesis Program

Another and more immediately applicable approach to paraplegia is the development of an electric "by pass" of the injured cord by stimulation of paralyzed muscles. This is accomplished through electrical signals derived from electrical activity of the brain or of the remaining normal muscles. Since the muscles of paraplegics are usually intact, it is theoretically possible to activate them in a coordinated manner by electrical signals derived either directly from the brain or from the muscles of the unparalyzed part of the body.

The electrical "by pass" approach to the problem of paraplegia is being actively pursued in the Laboratory of Neural Control. This laboratory is studying the nerve cells in the brain and spinal cord which control the muscles of the body with the specific aim of effectively "by passing" breaks in the spinal cord. The Laboratory of Neural Control also monitors a contract program for developing prostheses for the neurologically handicapped, including paraplegics. Two such contracts at the University of California at San Francisco and Duke University, Durham, North Carolina, were recently initiated to develop a neuroprosthetic device for bladder control, and preliminary results appear to be quite promising. The paralyzed bladder is a major problem of paraplegia. Although about fifty percent of all paraplegics somehow retain the ability to empty their bladders even though contact between brain and bladder has been traumatically disconnected, the other half face the prospect of premature death from renal infection. Additional studies on more effective ways to control both the urinary bladder and large bowel are being supported through the Institute's extramural programs.

Angiography of Acute Spinal Cord Injury

For a number of years scientists in the NINDS Neuroradiology Section at the NIH Clinical Center have been carrying out selective angiographic studies of the spinal cord and have developed techniques of visualizing the cord's blood vessels into a reliable diagnostic tool in cases of spinal cord arteriovenous malformations.

Gradually, the use of these techniques has been expanded to patients with spinal cord pathology other than arteriovenous malformations, such as tumors, syringomyelia, and secondary dilations of the spinal cord vessels.

Although application of arteriography to acute spinal cord injuries is just now beginning, its potential importance can hardly be overestimated because of the crucial role of the vascular components in the development of post-trauma damage and the recovery from such damage.

In a recent study, the cord vessels of six patients with acute cervical spine injury were demonstrated angiographically. Arteriography was carried out at different intervals after trauma, in two instances within six hours. Although the angiographic findings in these patients probably did not change the final outcome, they did affect therapeutic management in at least three cases. In one patient a decision not to operate was made on the basis of the angiography. In two other patients, the angiography coupled with other criteria, determined the type of surgical approach.

Investigators working in this area believe that angiographic observations, when taken in concomitance with the degree of bone-ligament alignment and the subsequent clinical course, tell a good deal about the pathophysiology of certain cord injuries. It is anticipated that in the near future arteriography will be able to establish the presence of intraspinal or intramedullary bleeding, cord transection, and the degree of cord edema. This will undoubtedly help in the prognostic assessment and management of spinal cord injured patients.

Head Injury

Research in head injury is a major interest of the NINDS, which is currently supporting three Head Injury Research Centers, 13 related research projects, and a small intramural program at the NIH Clinical Center. These studies receive input from a variety of disciplines, including neurosurgery, neurophysiology, neuropathology, anesthesiology, nuclear medicine, and biomedical engineering. At present the program is oriented toward solving the more fundamental neurologic problems in head injury rather than those of logistics, safety, and similar concerns. For example, a severe blow to the head produces, in addition to the obvious effects, profound alterations in the second-to-second regulatory and nutritional chemical processes within and between brain cells. These alterations, and in fact the processes themselves, must be understood before much can be done to reduce or ameliorate the effects of an injury, and to salvage brain cells.

A head injury may stop or reduce a victim's breathing. Knowing precisely how ischemic brain hypoxia (lack of oxygen) brings about deterioration of nerve cells could enable scientists to find ways of effecting at least some and possibly a substantial degree of salvage. A blow to the head often causes edema--swelling--within the skull, and devastating pressure on the brain, since there is no way for it to expand outward. Again, the chemical mechanisms causing the edema, if better understood, could be better controlled. The brain controls, or participates in control of, virtually every vital bodily function--breathing, the heart beat, temperature regulation, and so on. The fine details of these systems must be known for treatment to advance beyond the empirical stage, and find an adequately grounded rationale.

The Institute-supported Head Injury Research Center at the Cincinnati General Hospital, is studying the latter problem--"the effects of intracranial trauma on systemic function." Brain injury and systemic disturbances often "feed" each other, as in cases where the injury causes pulmonary edema, which in turn causes oxygen lack in the brain, compounding the damage. Sometimes brain injury causes release of antidiuretic hormone, which adds to the problem of water retention (edema). The Cincinnati scientists are approaching the overall problem in both aspects.

Another Institute-supported center at the University of Chicago is studying, in animals, the ultrastructural, biochemical, and physiologic changes that occur during head injury. The scientists are producing nerve damage by various methods, including gunshot wounds, clamping of arteries, and sudden compression of the spinal cord, and measuring changes in phospholipids, gangliosides, and other substances. Finding that an immediate decrease in blood flow is a striking result in several types of head injury, this group is seeking to determine whether the cause is a stretch reflex of the vascular muscles, a nerve impulse, or release of a chemical compound. Testing various drugs in the experimental animals, the group has found that dimethyl sulfoxide, a controversial drug tried and abandoned some years ago in mental retardation, may be potentially useful. The compound is thought to stimulate respiration and have diuretic action.

Scientists at a center at the University of Texas Medical Branch, Galveston, have worked out a practical method for continuous monitoring of intracranial pressure in head injury patients. The method entails use of a transducer inserted through a small hole in the skull, and will be combined with telemetry. Sometimes vital signs such as heart rate and respiration are affected by the methods used to measure them, and the scientists are seeking to minimize this "perturbation response" by use of automatic monitoring equipment. Also within this project are studies of cerebral autoregulation in both patients and primates; efforts to refine definition of brain death, and evaluation of steroid drugs in head injury.

Brain hypoxia (oxygen deficiency) is the general target of a group of scientists at the University of Pennsylvania. Since the majority of head injury patients who survive to reach the hospital do not have primary irreversible brain damage, and since hypoxia may convert a reversible process into a lethal one, the group is seeking to ascertain whether hypoxia is the common denominator as the cause of death in head injuries, and what approaches they might take to the problem. Studies with patients include measurement of oxygen and glucose metabolism in the brain, intracranial pressure, and regional blood flow measurements before and after treatment with steroids, diuretics, hyperventilation, and hypothermia. Patients requiring exposure of the brain are studied by surface fluorometry. Parallel studies are also in progress with experimental animals.

A New York University team has also been studying cerebral blood flow and oxygen metabolism after head injury. An important contribution of this group has been the development of clinical mass spectrometry for monitoring blood flow and oxygen consumption on a continuing basis.

Supplementing the team approach to brain injury reflected in the centers, grantee scientists are working in various universities and hospitals on generally smaller, more circumscribed research projects. Examples of these are electron microscope studies of nerve tissue in experimentally injured animals that are particularly suitable, such as the mongolian gerbil; study of the formation of new corticospinal connections after various destructive surgical procedures within the brain; and efforts to refine ultrasound for visualization of tissues when portions of the skull have been removed to relieve edema.

A number of projects relate primarily to edema (swelling), which, as noted above, is one of the chief problems in head injury. Movements of cerebrospinal fluid under normal and altered conditions are under study, as are the roles of hormones and neurotransmitters.

NINDS neurosurgeons have had a long-term interest in brain injury, and have both conducted and monitored contract-supported animal studies of torsional stress in the neck, with a view toward development of better safety helmets.

A new Section on Head Injury and Stroke, within the Institute's Applied Neurologic Research Branch, Collaborative and Field Research, administers several contracts for work in head injury, including a study of cerebral blood flow in coma, and a long-term neuro-psychological study of recovery after the acute care phase has passed.

The knowledge that irreversible brain damage in survivors is usually a result of the aftereffects of the injury rather than the injury itself makes a concerted attack in this area of neurology immensely worth while. From such an effort can flow many possible improvements in the handling and management of accident victims at the scene, as well as improvements in emergency room procedures which can result in the saving of tens of thousands of lives.

HEALTH SERVICES ADMINISTRATION

Maternal and Child Health

Children receiving health services in FY 72 from Title V assisted State Crippled Children's Programs included 95.5 with spina bifida and/or myelomeningocele. Of these, 19.7% or 1,876 were new cases referred that year. These children frequently require a range of services including hospitalization, treatment by a variety of medical specialists, and services from many health professions including nursing, social work, and physical and occupational therapy. Some children with spinal cord injuries also received services from the State Crippled Children's Programs. In general these efforts are directed towards helping the child achieve optimum function and are not those purely of maintenance.

Title V funds also support training and demonstration projects which provide model care for children with these conditions. Two projects, "The Project for Children with Handicapping Conditions," Dr. Mary Ames, the Children's Hospital of Philadelphia, and "Spina Bifida Demonstration and Service Clinic," Dr. Chester Swinyard, New York University Medical Center, have nationwide recognition for the care of these children and training of professionals to care for them. Many other Title V supported multidisciplinary clinics for handicapped children include children with spinal disorders in their caseload.

Some of the Title V research projects on the care of children with multiple handicaps have included children with myelodysplasia. One currently underway, "Cost and Utilization Patterns of Rehabilitation Service," Dr. David Macfarland, Crippled Children's Division, University of Oregon, includes an analysis of the total costs of care to the families of children with myelomeningocele. One project supported by the MCH special foreign currency program at the Institute of Mother and Child, Warsaw, entitled "Medical and Social Rehabilitation of Children with Myelomeningocele" demonstrated the need of a multidiscipline team for such cases.

UTILIZATION OF RESTORED 1973 FUNDS

Mr. Flood. I want a breakdown of the $23,269,000 of 1973 funds obligated in 1974, with a description of how those funds will be used; then an identification of the amounts involved in 1974 obligations for multiple-year funding, research grants and contracts, both.

Then in your Institute, on page 232 of the justifications, include the 1973 appropriation restorations to reflect that 2-year funding of the grants.

That is not as tough as it sounds.

Dr. Tower. We have most of it already and will be very happy to supply it.

[The information follows:]

Obligations by Budget Mechanism
Showing "True" Program Levels
in 1974 - 1975
(Amounts in thousands)

Budget Mechanism	1972		1973		1974		1975	
	No.	Amount	No.	Amount	No.	Amount	No.	Amount
Grants								
Regular								
Non-competing	814	# 37,612	742	# 38,151	622	# 36,468	821	# 50,579
Competing	213	11,234	135	10,174	391	24,615	300	16,826
New	188	7,990	114	6,161	367	14,663	220	3,900
Supplemental	(161)	1,618	(226)	2,673	(109)	1,466	(107)	1,250
Subtotal	1,215	58,454	991	57,159	1,380	77,212	1,341	72,555
Special								
Specialized Research Centers		5,691		5,690		5,691		5,691
Scientific Evaluation	--	--	--	--	--	152	--	178
Research Career Program	78	1,755	65	1,395	79	1,688	86	1,793
Subtotal	78	7,446	65	7,085	79	7,531	86	7,662
Total Grants	1,293	65,900	1,056	64,244	1,459	84,743	1,427	80,217
Fellowships								
Non-competing	20	135	31	277	22	271	201	3,009
Competing	27	214	3	25	--	--	--	--
New	69	674	24	197	200	3,000	29	432
Supplemental	(9)	4	(25)	10	--	--	--	--
Subtotal	116	1,027	58	509	222	3,271	230	3,441
Training Grants								
Non-competing	212	9,116	227	9,766	236	9,761	98	3,715
Competing	93	3,596	32	1,645	10	782	--	--
New	75	1,381	27	359	8	415	--	--
Supplemental	(28)	192	(23)	69	(202)	2,363	--	--
Subtotal	380	14,285	286	11,839	254	13,321	98	3,715
Laboratory & Clinical Research	--	10,701	--	10,434	--	12,521	--	13,343
Research & Development Contracts	67	8,260	52	8,104	97	9,240	103	10,692
Collaborative Research & Support	--	7,039	--	6,547	--	7,796	--	8,065
Biometry, Epidemiology, & Field Studies	--	--	--	--	--	--	--	--
International Center	--	--	--	--	--	--	--	--
Research Management & Program Services	--	4,087	--	3,681	--	4,328	--	4,390
TOTAL	--	111,299	--	105,358	--	135,220	--	123,863

Obligations by Budget Activity
Showing "True" Program Levels
in 1974 - 1975
(Amounts in thousands)

Budget Program	1973		1974		1975	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Communicative Disorders........................	8	$13,595	8	$17,793	8	$15,529
Neurological Disorders........................	178	53,232	167	63,335	167	56,747
Stroke, Nervous System Trauma..................	6	12,978	6	22,633	6	20,104
Fundamental Neurosciences......................	6	10,707	6	13,613	6	12,585
Intramural Laboratory & Clinical Research.......	242	6,456	242	7,684	242	8,233
Research Management & Program Services..........	94	8,390	91	10,162	91	10,665
TOTAL..	534	105,358	520	135,220	520	123,863

Multi-year Funding from
1974 Appropriation
(Amounts in thousands)

Budget Mechanism	No. of Awards	Total Amount	Amount Affecting 1975 Funding	Remarks
Research Grants..................	17	$1,030	$515	Communicative Disorders
	43	2,599	1,300	Neurological Disorders
	28	1,654	827	Stroke, Nervous System Trauma
	12	717	358	Fundamental Neurosciences
	100	6,000	3,000	Total
Research & Development Contracts.	3	700	330	Communicative Disorders
	4	975	415	Neurological Disorders
	2	320	160	Stroke, Nervous System Trauma
	9	1,995	905	Total

Distribution of 1973
Impounded Funds
(Amounts in thousands)

Budget Mechanism	No. of Awards	Amount	Remarks
Research Grants......................	26	$1,980	Communicative Disorders
	64	4,995	Neurological Disorders
	41	3,179	Stroke, Nervous System Trauma
	18	1,377	Fundamental Neurosciences
	149	11,531	Total
Fellowships.........................	1	10	Communicative Disorders
	2	30	Neurological Disorders
	1	10	Fundamental Neurosciences
	4	50	Total
Training Grants.....................	8	1,364	Communicative Disorders
	20	3,262	Neurological Disorders
	3	478	Stroke, Nervous System Trauma
	2	217	Fundamental Neurosciences
	33	5,321	Total
Research & Development Contracts.....	1	218	Communicative Disorders
	6	848	Neurological Disorders
	1	216	Stroke, Nervous System Trauma
	1	235	Fundamental Neurosciences
	9	1,517	Total

SPEECH, HEARING, AND LANGUAGE DIFFICULTIES

Mr. **Flood**. How many Americans have speech, language, and hearing difficulties?

Dr. **Tower**. It is about 23 million, sir.

Mr. **Flood**. When do you plan to increase the research in voice rehabilitation, the early detection of that disease of the larynx, a terrible thing? Do you have any current plans?

Dr. **Tower**. Yes, sir, we have some plans for that. It is a little early to give you any specifics on that, but this is an area in which both our council and the new appointees hired for our laboratories are working now.

Mr. **Flood**. What about the meeting down at the University of Florida? Do you have any plans to implement the recommendations of the NINDS-sponsored conference on early detection of larynx disease? Is there anything to implement that? What happened?

Dr. **Tower**. We have received some of their recommendations and we are in the process of stimulating the proper work both in the grant and contract area.

Mr. **Flood**. Do you have any plans for electrodes to help the profoundly and totally deaf?

Dr. **Tower**. We have a very active program both on campus and contractually in this whole field, including the important area dealing with electrodes stimulating either the inner ear itself or the nerve coming out from it.

MIDDLE EAR DISEASES

Mr. **Flood**. You hear a lot about the flu and congestion in the middle ear.

Dr. **Tower**. Yes.

Mr. **Flood**. Is that research going to include prevention and treatment of chronic inflammatory diseases of the middle ear and the mastoid, as distinguished from the flu?

Dr. **Tower**. This is one of the most serious problems we have, and we have several groups which are being strongly supported to deal with this problem. One in Minnesota, for example, where this is their main point of research attack.

NEURO-OTOLARYNGOLOGY LABORATORY

Mr. **Flood**. Last year my distinguished colleague, Mr. Michel, asked you to comment upon the laboratory for neuro-otolaryngology and you didn't sound very optimistic. What is your forecast now?

Dr. **Tower**. We have activated that laboratory—our local people on the campus are renovating the laboratory area at the moment, and we hope by the first of July it is going to be in full-scale research.

Mr. **Flood**. We hope you get your hope.

Dr. **Tower**. If not, somebody is going to hear from me, sir.

Mr. **Flood**. And you will have some company.

Mr. Conte.

Mr. **Conte**. Thank you, Mr. Chairman.

I want to take this opportunity to congratulate Dr. Tower for being nominated as the new Director. In looking over his résumé I see that he brings a great deal of talent and outstanding background to the Institute and I am sure it will be in good hands.

Dr. TOWER. Thank you.

CHILDHOOD AND ADULT NEUROLOGICAL DISORDERS

Mr. CONTE. In your program descriptions, you divide neurological disorders into childhood and adult disorders. Is this really a valid division?

Dr. TOWER. To some extent, yes. There are many diseases of the nervous system particularly common during childhood, and when they occur, that is when the most serious problems develop. The reason for it being so important is that the human brain continues to grow at least until age 6 years. A disease hitting the nervous system during the time of development can be much more devastating than it is when the brain is mature. This is particularly true in areas of mental retardation, cerebral palsy, and that sort of thing. It becomes almost a subspecialty in itself.

As you are aware in clinical practice we have pediatric neurologists precisely because of this kind of problem.

FUNDAMENTAL NEUROSCIENCES

Mr. CONTE. The fundamental neurosciences get only 10 percent of your total budget. Is your advisory council specifically aware of this?

Dr. TOWER. Yes, sir, it is aware of it. We feel that is a very important area to support. Let me explain it this way, sir. It is not only in that category that we are supporting fundamental neuroscience. That 10 percent represents those areas of the neurosciences which are not easily identified with one of the other program areas such as neurology, stroke and trauma, communicative disorders. Within those others there are also fundamental neuroscience projects being supported which bear directly on a particular disease problem even though it is at the fundamental level.

So, for example, some of the research in virus diseases of the nervous system may appear programmatically within neurological disorders, whereas other studies related to the fundamental nature of viruses and how they interact with membranes and that sort of thing might appear in the fundamental neuroscience category. So it is a little bit deceiving to make that particular distinction, but we needed some category where we could put those projects that weren't directly disease related.

RESEARCH ON SLOW AND LATENT VIRUS

Mr. CONTE. For the record, will you provide a breakdown of your research efforts on slow and latent viruses showing research grants, contracts, intramural studies, and any other efforts, giving number of projects and dollar amounts?

Dr. TOWER. Yes.

[The information follows:]

NINDS RESEARCH EFFORTS ON SLOW AND LATENT VIRUSES

The main in-house research effort devoted to slow and latent viruses is centered in the Institute's Laboratory of Central Nervous Systems Studies. This laboratory includes 21 full-time permanent employees and 10 temporary employees with a total yearly operating cost of approximately $1,784,000. Includes in this cost are the following four contracts:

1. Animal holding contract at Otisville, N.Y.	$117, 000
2. Animal holding contract at Gulf South La	518, 000
3. Department of Defense maintenance contract at Ft. Detrick	194, 000
4. Operational contract with NCI for support cost at Ft. Detrick	155, 000

NUMBER AND AMOUNT OF GRANTS ON SLOW AND LATENT VIRUSES BY TYPE

	Number	Amount
Research grants	20	$1, 869, 000
Training grants	1	36, 000
Traineeships	4	67, 000
Fellowships	5	102, 000

NEUROSCIENCE RESEARCH GRANTS

Mr. CONTE. How many research grants do you intend to award in 1974 and 1975 in the basic neurosciences?

Dr. TOWER. I would just have to give you a guess and I would like to be able to provide you with a more accurate figure for the record. But I would guess offhand that the number would be somewhere in the order of 50 or 60 each year.

[The information follows:]

It is planned to award 50 research grants in 1974 and 52 research grant in 1975 for basic neurosciences.

MANPOWER SHORTAGES

Mr. CONTE. Yours is one of the few health budget justifications we've seen that admits to trained manpower shortages. In what fields are the needs greatest?

Dr. TOWER. You are referring to the communicative disorders where I made that statement?

Mr. CONTE. Yes.

Dr. TOWER. I made that quite specifically because we are aware, in that area, of a relatively significant lack of what we call bench scientists. When we look over the kind of grants that we are supporting we make a distinction between clinically-oriented investigation and basically-oriented investigation, and we find that there is a rather significant lack of the latter in the area of communicative disorders.

We have looked to see why that is so. We find that there are relatively fewer scientists at the bench looking at fundamental problems in this area than there are in the other program areas, and that is why we think there is a need to train more people. We are just not generating the kind of undergirding that is needed to get at many of the clinical problems, and, as you are aware, this is a very vast area with an enormous number of problems subsumed under the term "communicative disorders."

HEAD INJURIES

Mr. CONTE. Have you developed or are you developing any research on head injuries in connection with emergency medical services which Congress has recently expanded?

Dr. TOWER. This is a question which I think is a very good one, sir. We have been quite concerned about this recently. I have to answer you we are not doing as much as I think we should be doing. We have had some conversations, for example, with people in the New York area where they have developed a very active program recently for coordinating all of these activities, and some of our very good friends up there in the neurological community have alerted us to the necessity of doing this and we are looking actively into it.

I think it is very important. We would actually like to see more activities going on in relation to head injuries because that becomes a very important problem. It is part of a general problem of trauma since head injury, after all, is not the only thing you may suffer in the accident. It is one of the more important ones I agree. We are working on it.

FELLOWSHIPS AND TRAINING GRANTS

Mr. CONTE. Looking at page 250 of your justification I see that your objective for 1975 is 18 fellowships and 6 training grants in the fundamental neurosciences. It is hard to believe those figures since work in the fundamental neurosciences is basic to not only all the rest of your work but much of that of other institutes as well. Were those objectives given to you, or did you arrive at them through some estimating process?

Dr. TOWER. This represents in part our projections of what we expected would come on the basis of past experience, partly what it looked as if the budget would allow for us to plan for. I think this is a question that is kind of open-ended. You can take many positions within it, and certainly my feeling is that we need to support as much basic science research and training as we can justify in terms of its meritorious nature. There is a great deal still to know.

Mr. CONTE. Would you say that if you had more money you could expand in this particular area?

Dr. TOWER. We could, yes, sir.

NEUROIMMUNOLOGY LABORATORY

Mr. CONTE. Is your laboratory of neuroimmunology planned for 1975 or 1976?

Dr. TOWER. Hopefully for 1975. This depends primarily on recruitment. I have a very good person whom I am actively recruiting now and if I can get him in hand, it will be 1975.

Mr. CONTE. How many staff do you plan to add for the new lab?

Dr. TOWER. The plans in discussing with him would begin at about 10 people altogether.

Mr. CONTE. What is your total budget estimate for the lab?

Dr. Tower. It would be somewhere in the order of between $350,000 and $500,000.

Mr. Conte. Do you maintain any joint laboratories with other Institutes?

Dr. Tower. Not in the specific sense of being joint laboratories, but we have a great deal of collaboration in various areas, particularly in the infectious disease area where we collaborate with the Cancer Institute, with the Allergy and Infectious Diseases Institute, and to some extent with the Child Health Institute.

EPILEPSY

Mr. Conte. In your statement on a new drug for epilepsy, you say "Major achievement this year has been the introduction of the new anticonvulsant drug, carbamazepine, the first new drug for epilepsy to be approved in 14 years." Is that on the market now?

Dr. Tower. Yes, sir; it has been approved by the Food and Drug Administration and is on the market now.

Mr. Conte. I know some of my constituents would be really pleased to hear that. I know some families that have children who are epileptic and up to now there hasn't been very much to help them.

Dr. Tower. We hope there will be some more new drugs. We have three or four potential ones right now.

Mr. Conte. Thank you, Doctor. It is a very fine statement and very fine answers.

Mr. Flood. Mr. Patten.

Mr. Patten. Doctor, it is a pleasure to have you here.

You spoke of one of your 13 major programs for learning something about the brain and strokes, that included in the nerve system is an automatic control of body temperature.

Dr. Tower. Yes, sir.

Mr. Patten. Do you think the body has a thermostat?

Dr. Tower. It definitely does.

Mr. Patten. Where, right here?

Dr. Tower. You go in a little further than that, yes, sir. It is right about in the middle of the brain.

Mr. Patten. I had an infection in the forehead and some doctor went through a bone in my forehead and I think he spoiled my thermostat. I am a sissy when it comes to a draft ever since.

It is a pleasure to visit with you. This concerns all of our citizens. But the questions put forth for our purpose of looking at your budget have been ample, and on account of the hour I will not pursue this. That is not to be construed by any means this work is not highly important to all of our people.

I seldom go home I don't visit the hospital, the intensive care section. It continues all the time. Many people have their prayers with you.

Dr. Tower. Thank you.

Mr. Flood. Mr. Robinson.

Mr. Robinson. Thank you, Mr. Chairman.

I would also like to congratulate you on the fact that at long last you are taking over the reins of this Institute formally and I think it is overdue.

MULTIPLE SCLEROSIS

I am particularly interested in multiple sclerosis and I have noted carefully both what you said in your statement and in the justification with regard to this matter.

You say that the Advisory Commission's report is under careful study. You mention that this year NINDS will fund four clinical research centers and eight program projects, and in your justifications you mention there will be 65 research projects related to multiple sclerosis.

Dr. Tower. Yes.

Mr. Robinson. Since you also say the Commission's study is still under careful study, to what extent are the project areas related to the Commission report since this is not yet published? I know you are familiar with it, but it is not yet published.

Dr. Tower. If I may correct you, the report is published, it is available. It was presented both to the Secretary and to the Congress, and I think we therefore can say in that sense that it is published.

Really to say the report is under study reflects those areas where there might be some difference of opinion about how best to implement the recommendations and this sort of thing. I don't think that any of us have any quarrel with the basic approaches, the basic recommendations. And I think I can quote the Secretary who spoke to the Commission when they presented him the report and said he thought it was a very responsible report, well documented, and this was the kind of report that was extremely helpful to everybody because one could see precisely how the recommendations were arrived at.

Mr. Robinson. You feel then your fiscal year 1975 budget does take into consideration the implementation of the report to the extent it is reasonable and practicable to do so?

Dr. Tower. Yes, sir. As you understand there is a certain lag period when these reports come out before you can generate the maximum efforts that will be forthcoming. I am sure there will be a lot. This is the area many people are interested in right now.

EPILEPSY

Mr. Robinson. With regard to epilepsy and to carry one step further the query of Mr. Conte, you say that "Rational effective management of epileptic patients is now a reality."

What about the cost of this treatment? Is this going to be reasonable, Doctor, based on the drug you mentioned as being very promising?

Dr. Tower. I think the cost is reasonable, but, Mr. Robinson, as you are aware many epileptics are in low income groups, and they cannot themselves very often earn an adequate living because of their seizures and because of restrictive legislation in States and that sort of thing. So that cost is a problem for the epileptic patient.

The Epilepsy Foundation and other lay groups have devoted a fair amount of their funds and efforts to trying to obtain cheaper medication or free medication for those who cannot afford it at all. So that even though it may seem to us the cost of these medications are reasonable, it is not so to a lot of people.

SPINAL CORD INJURY

Mr. Robinson. The question of head injuries arose and that brings to my mind the question of spinal cord injury because so often they seem to associate. What about the claims we were hearing at one time, and still hear to some extent, that so many spinal cord injuries are exaggerated by improper handling of accident cases. Is this still a concern?

Dr. Tower. Yes, sir, it definitely is. Very often it is not apparent that a serious injury has occurred to the spinal column. Patients are not properly handled largely through ignorance of those who are trying to be helpful but have not been properly instructed in how to protect particularly the neck. This is the most serious problem I think. As a result further injuries can occur.

If I may cite an example which is familiar to all of us of Governor Wallace. When he was shot of course the most immediate problem was to deal with internal bleeding in the abdomen and he had to be positioned in such a way there is a real question that perhaps more damage was done to his spine before they were able to get to the bullet lodged there. This is an example of the kind of multiple problems you have.

So this is definitely a very serious concern, and we feel that the centers that we are establishing and the information that they will disseminate will be helpful. But obviously we need more of this.

I might say that the Paraplegia Foundation and the many people interested in paraplegia are very active in this area.

DEAFNESS

Mr. Robinson. One final question concerns deafness. I have a large family, and I know how noisy things can get around the average household and how the entertainment areas are so noisy today. I wonder to what extent we find an increase, if any, in the incidence of deafness among young people as a consequence of this. We have talked about it before here and I wonder if it still is a concern?

Dr. Tower. Yes, it is definitely a concern. We don't have the answer but we are very definitely concerned about it and we are looking at it. Dr. Lois Elliot, whom we have brought on to deal with our tract program particularly, has a special concern in the area and she has several contracts that will be let during the next year to examine this question, specifically addressed most to the point of whether there is a special problem with children particularly during the early years that they may be more sensitive to sound than we as adults, or vice versa. We really don't know the answer to that yet, and we think it is important to find out for precisely the reason you raise the question.

Mr. Robinson. Thank you very much.

Mr. Flood. Will you go beyond that and embrace the entire spectrum of noise as a pollutant? I am being very careful of my language when I say "pollutant."

Dr. Tower. Yes, sir, you are right.

Mr. Flood. Give that a real going over and come back to us with a full dress report on noise.

[The information follows:]

CURRENT NINDS RESEARCH ON NOISE

NINDS support of research on the effects of noise exposure has continued for a number of years through the extramural grant program. These studies, concerning both biologic effects of noise on the auditory system and human responses to noise, constitute the forefront of presently available data.

Several laboratories are presently conducting research on the basic mechanisms of destruction of the cochlea (or inner ear) resulting from exposure to noise. Procedures have been developed for using animals in this work since the recordings are made of the electrical responses of cells and histological analyses of cellular tissue can be completed. This means that investigators have also needed to develop procedures for obtaining "hearing tests" from these animals so that the perceptual effects of noise damage could be studied together with the physiological effects. One grantee has demonstrated that levels and durations of noise which do not produce lasting impairment in behavioral response to pure tone (no lasting effect on the "hearing test") are nevertheless sufficient to produce considerable cellular damage to the cochlea. In addition to research on the physiological damage incurred to the hair (or receptor) cells of the cochlea, investigators are attempting to understand the exact process by which this happens. For example, it is not clear whether exclusively mechanical factors are involved in destroying the receptor cells or whether biochemical or bio-electrical factors must also be considered.

Another area under investigation is the relationship between temporary shift of the auditory threshold resulting from noise exposure and permanent noise-induced hearing loss. One investigator has anticipated that measurement of temporary threshold shift in human populations exposed to noise might warn of impending permanent hearing loss, but the usefulness of that diagnostic strategy is now being reconsidered.

A laboratory, which has used animal models in some of its work, has also performed experiments in which a human volunteer (in this instance, the investigator) has been exposed to low levels of noise for prolonged periods of time. This permitted a study of the recovery of auditory sensitivity following the noise exposure. The importance of this work is related to the need for understanding the cumulative effects of exposure to moderate noise levels for periods up to 16 and 24 hours per day (where there might be insufficient recovery or quiet time prior to return to the noise environment). Finally, a grantee has conducted considerable research on the interfering effects of noise on speech and has attempted to derive equations for predicting these interfering effects from physical measurements of the noise.

Our Directed Research Program on Communicative Disorders is this year beginning several activities concerned with noise. These are described below.

Through an interagency agreement, NINDS has requested the Committee on Hearing and Bioacoustics (CHABA) of the National Research Council-National Academy of Sciences to help us in the review of existing information and in planning research concerning effects of noise on children. Types of questions which will be considered in this interdisciplinary planning activity include:

> Do children have the same susceptibility to noise-induced hearing impairment as adults or are they more or less susceptible?
>
> Among children is there any interaction between middle ear disease and noise exposure which would result in increased susceptibility to noise-induced hearing loss?
>
> Among children is there any interaction between general health and/or nutrition and susceptibility to noise-induced hearing loss?
>
> Is environmental noise ever a causative or contributing agent for mental illness in children?

CHABA will produce two documents under this interagency agreement. The first will be a critical review, analysis, and synthesis of existing data concerning both auditory and extra-auditory effects of noise on children while the second will be an examination of possible research strategies for obtaining better understanding in this area. (Although we consider these questions extremely important, the need to implement research without placing children at risk requires extra planning.) Our plan calls for completion of both these documents by late December 1974, after which we will advertise selected research strategies for competitive bid. The documents, themselves, will also be made available to the scientific community.

A second directed research activity initiated this year is development of a new test of speech discrimination in noise. Unfortunately, pure tone tests of auditory sensitivity (i.e. audiograms) do not allow adequate prediction of the possible "handicapping" effects of hearing loss, and discrimination of speech is particularly difficult to predict because of the cognitive components of the task. The new test, consisting of sentences presented against a noise background, will be used to determine the extent of understanding of "everyday speech" among persons with noise-induced hearing loss and is expected also to be useful in the fitting of hearing aids for persons with other types of acquired hearing loss. The Request for Proposals for this work was advertised during the winter and proposals are now under review.

One additional research activity should be mentioned in this context. NINDS has developed a wearable master hearing aid which permits study of the effects of a variety of electroacoustic parameters of hearing aids while the patient goes about daily activities. This year, NINDS will fund a contract which will use these master aids to develop prototype procedures for fitting hearing aids to persons who typically do not find aids satisfactory. We anticipate that these procedures may also assist hearing-impaired patients to deal better with a noisy environment and, of course, be of considerable help to persons who have already experienced noise-induced hearing loss.

NINDS cooperation with other agencies

NINDS assumes an active initiative in coordinating its research with other agencies. Development of the five-year plan of our directed research program in Communicative Disorders was facilitated by conversations with investigators active in the noise research field in that pressing research needs were addressed and duplication with other agencies was avoided. We expect to formalize our communication channels with the other Health, Education, and Welfare (HEW) institutes concerned with noise research (NIEHS and NIOSH) and anticipate mutual planning benefits by all three institutes. In addition, NINDS participates actively in the Health Effects Panel (HEP) of the EPA's Office of Research and Development (ORD) which is attempting to maintain an overview of all federally supported research on noise and health effects. The formalization of the health effects panel has rounded out the NINDS dialogue with other agencies and we expect to continue our support of these coordination efforts.

Future NINDS plans

Three research areas which NINDS hopes to address, beginning in FY 1975, are concerned with preventive approaches; two of these deal with auditory effects of noise and one with extra-auditory effects. A fourth anticipated research area will be directed at ameliorating the handicapping effects of noise-induced and other types of hearing loss.

Through its grants program, NINDS has supported almost all of the studies in the United States on the relationship between noise exposure and resulting hearing loss and most proposed regulations are based on the results of these studies. However, the available data are concerned primarily with noise exposures of eight hours duration; insufficient information is available concerning the effects of noise exposures of less than eight hours duration or of intermittent exposures. Our advisors have suggested that a number of large industries are likely to have records containing the necessary information for studying the relationship between either of these two durations of noise exposure and resulting hearing loss. The challenge is to design the type of contractual arrangement (either competitive bid or single source) which would convince such industries to share these data with us. We intend to devise the plan and design for accomplishing these studies during FY 75 and to arrange full implementation during FY 76. Resulting data and conclusions will be made available to EPA, the Occupational Safety and Health Administration of the Labor Department, and others for use in reviewing noise standards then extant.

A second research topic which NINDS proposes to address concerns the great variability in individual susceptibility to noise-induced hearing loss. As one scientist has remarked in print, a standard at 85 decibels (A scale) for eight hours exposure to noise will fail to protect between 2 and 20% of the population from noise-induced hearing loss depending on which set of data one selects. Since the issue of individual differences has appeared in so many research studies, we believe that it would be worthwhile to investigate other causative agents which may be interacting with the noise exposure to produce these differences. For example, studies in the research literature already document the interaction between certain ototoxic drugs (such as kanamycin) and noise exposure in animals that lead to greater loss than would have been expected had the effects of each agent been simply additive. We believe it is possible either that certain nutritional or metabolic deficiences may predispose an auditory system to damage by less intense noise levels or that these other agents interfere with the recovery process of the auditory system from what in other individuals would be only temporary effects of noise exposure. We do not delude ourselves that these will be easy questions to answer, but we feel that the expertise available to us within NINDS and NIH will facilitate the task. We intend to initiate planning of this work during FY 75 and to implement it fully in FY 76.

The third topic concerns the suggestion that chronic health problems in humans may be caused by moderate noise levels [70-90 decibels (A scale)] which continue for long durations. Evidence is limited and controversial with respect to extra-auditory health effects of noise, as derived from several European and one United States study of human subjects receiving industrial noise exposures and from experiments on lower animal species. NINDS is considering the implementation of directed research on selected aspects of this problem. Both epidemiological studies of human populations, with particular attention to inner city, very young, and geriatric populations, and animal experiments are currently being contemplated. Since this would be a major undertaking, requiring several years and a sizeable expenditure before even preliminary results would be forthcoming, NINDS feels that careful planning is first required.

The fourth planned topic concerns research on the auditory capabilities of persons with hearing loss due to aging (presbycusis) or with noise-induced hearing loss. These people have special difficulty understanding speech when it occurs in a noisy background. Although some NINDS grantees have conducted research in this general area, available information is sparse. Needed is a well-planned parametric study in which auditory performance of individuals with this type of hearing difficulty is measured for a wide variety of tasks, including many tasks with noise present. Particularly important will be studying the same listener for as long as 3500-4500 hours (in sessions not exceeding 1-1/2 hours per day). There are a number of reasons for considering conduct of this research at our National Institutes of Health facilities where arrangements for recruiting appropriate subjects may be more easily made than at most academic institutions or hearing clinics. Data from these parametric studies will be used in designing "new generations" of hearing aids for hearing-impaired persons and will become background information for the future development of auditory protheses.

NINDS resources to carry out these plans

As we have described on another occasion, NIH research on communicative disorders has previously been carried out primarily via grants. This year, the new Laboratory of Neuro-otolaryngology has been established and the relatively new directed research program in Communicative Disorders has expanded from its previous attention exclusively to sensory aids for the deaf to additional emphases on disorders of speech and language and on noise. To carry out the future plans just described, additional resources (funds and staff) would be required.

Mr. Flood. Thank you.
Dr. Tower. Thank you.

JUSTIFICATION OF THE BUDGET ESTIMATES

NATIONAL INSTITUTES OF HEALTH

National Institute of Neurological Diseases and Stroke

Amounts Available for Obligation [1/]

	1974 Revised	1975
Appropriation	$125,000,000	$119,958,000
Amount withheld (PL 93-192)	-5,042,000	---
Subtotal, adjusted appropriation	119,958,000	119,958,000
Real transfer to:		
"Departmental Management" (For Department-wide reductions in public affairs)	-55,000	---
Comparative transfers to:		
"Office of Assistant Secretary for Health" (Transfer of administrative support activities to the Office of the Assistant Secretary for Health)	-63,000	---
"Departmental Management" (Transfer of accounting functions from the OS Working Capital Fund)	-7,000	---
Comparative transfers from:		
"National Institute of General Medical Sciences" (Decentralization of scientific evaluation grants program)	+152,000	---
"Departmental Management" (Transfer of indirect cost negotiation function to the OS Working Capital Fund)	+8,000	---
Subtotal, budget authority (base obligations)	119,993,000	119,958,000
Unobligated balance, restored	+23,269,000	---
Comparative transfer of restored unobligated balance to Research Resources for General Research Support Grants	-4,137,000	---
Total, obligations	139,125,000	119,958,000

[1/] Excludes the following amounts for reimbursable activities carried out by this account: 1974 - -$200,000; 1975 - -$200,000

Summary of Changes

1974 Estimated obligations..	$139,125,000
1975 Estimated obligations..	119,958,000
Net change..	-19,167,000

	1974		Change from 1974	
	Pos.	Amount	Pos.	Amount
Increases:				
A. Built-in:				
1. Within grade salary increases..	--	--	--	+$258,000
2. BEC rate change................	--	--	--	+6,000
3. Service and supply fund........	--	--	--	+129,000
4. FTS...........................	--	--	--	+5,000
5. One extra day of pay...........	--	--	--	+45,000
6. Annualization of 1974 pay increase in 1975.............	--	--	--	+263,000
7. Payment to NIH Management Fund for centrally furnished services....................	--	--	--	+247,000
Subtotal...	--	--	--	+953,000
B. Program:				
1. Research Grants:				
a. Non-competing continuations.	--	$36,468,000	--	+28,143,000
b. Competing..................	--	--	--	+21,976,000
c. Special....................	--	7,531,000	--	+131,000
2. Fellowships....................	--	3,271,000	--	+170,000
3. Intramural laboratory and clinical research............	242	7,684,000	--	+218,000
4. Collaborative research and support.....................	187	6,955,000	--	+74,000
Subtotal...	--	--	--	+50,712,000
Total, increases.....	--	--	--	+51,665,000
Decreases:				
A. Built-in:				
1. Annualization of average grade reduction in 1973............	--	--	--	-20,000
B. Program:				
1. Research Grants:				
a. Noncompeting completed or converted to competing status...................	--	36,468,000	--	-17,032,000
b. Competing completed or converted to noncompeting....	--	--	--	-40,744,000
c. 1974 obligations used to fund 1975 continuations...	--	--	--	-3,000,000
2. Training grants................	--	13,321,000	--	-9,606,000
3. Research & development contracts	--	10,145,000		-358,000
4. Research management and program services....................	91	3,023,000		-72,000
Subtotal...	--	--	--	-70,812,000
Total, decreases......	--	--	--	-70,832,000
Total, net change......................	--	--	--	-19,167,000

Explanation of Changes

Increases:

A. Built-in:
1. Increase of $258,000 is for within grade salary increases of civil service employees provided by law.
2. The increase of $6,000 will provide for rate change approved for employee compensation.
3. The increase of $129,000 will support additional operating costs of the NIH service and supply fund.
4. An increase of $5,000 is requested for the additional cost of the Federal Telecommunications System.
5. In 1975 an amount of $45,000 is requested for one extra day over 1974.
6. An additional $263,000 is required for annualization of the October, 1973 pay raise.
7. "National Institutes of Health Management Fund" - The increase of $247,000 is for increased costs for centrally furnished services such as patient care, receipt and initial review of all grant applications, computer services, maintenace of buildings and grounds, custodial services, communications, and transportation.

B. Program:
1. Research Grants:
   a. The increases of $28,143,000 in noncompeting research grants represent the continuation of previously awarded grants plus "new" continuations increased by 99: from 622 in 1974 to 721 in 1975.
   b. The amount of $21,976,000 in competing research grants reflects: (1) $3,900,000 for 220 new awards (b) $16,826,000 for 300 competing continuations and $1,250,000 in supplementals.
   c. The increase of $131,000 reflects an increase of $26,000 for scientific evaluation and $105,000 for research career awards.
2. Fellowships - The increase of $170,000 includes $432,000 for 29 additional research training fellowship awards and an offsetting decrease of $262,000 for the phaseout of postdoctoral fellowships.
3. Intramural laboratory and clinical research - The program increase of $218,000 will support basic and clinical research in neurological and communicative disorders.
4. Collaborative research and support - A program increase of $74,000 will support the increased logistic cost associated with the Institute's collaborative programs.

Decreases:

A. Built-in:
1. The decrease of $20,000 is a result of the average grade reduction during 1973.

B. Program:
1. Research Grants:
   a. The decrease of $17,132,000 represents 307 noncompeting regular research grants that were completed in 1974 or that are being converted to competing status in 1975.
   b. The decrease of $40,744,000 reflects the completion or conversion of 698 competing grants to a noncompeting status.
   c. The decrease of $3,000,000 reflects the reduced funding required in 1975 due to the multi-year funding of 60 projects in 1974.
2. Training grants - The decrease of $9,606,000 is the result of the phasing out of the Institute's graduate training programs in 1975.

3. Research and development contracts - The decrease in 1975 of $358,000 will reduce the estimated number of contracts from 111 in 1974 to 101 in 1975.
4. Research management and program services - The decrease of $72,000 is the result of non-recurring cost in 1975 for the multiple sclerosis commission and the release in 1974 of 1973 impounded funds.

Obligations by Activity

Page Ref.	1974 Base* Pos.	1974 Base* Amount	1975 Estimate Pos.	1975 Estimate Amount	Increase or Decrease Pos.	Increase or Decrease Amount	
233 Communicative Disorders.........	8	$ 15,258,000 (18,830,000)	8	$ 14,391,000	--	-$867,000	A
235 Neurological Disorders.........	167	56,237,000 (65,372,000)	167	55,425,000	--	-812,000	B
238 Stroke and Nervous System Trauma.....	6	19,233,000 (23,106,000)	6	19,017,000	--	-216,000	C
241 Fundamental Neurosciences.....	6	12,132,000 (13,971,000)	6	12,227,000	--	+95,000	D
243 Intramural Laboratory and Clinical Research..........	242	7,032,000 (7,684,000)	242	8,233,000	--	+1,201,000	E
246 Research Management and Program Services.........	91	10,101,000 (10,162,000)	91	10,665,000	--	+564,000	F
Total obligations (base) Total obligations	520	119,993,000 (139,125,000)	520	119,958,000	--	-35,000	

Explanation of Changes

A) Communicative Disorders: The $867,000 decrease reflects an increase of $339,000 for research on improving the diagnosis, treatment, and prevention of diseases and disorders which affect the ear, nose and throat and hearing, language, and speech, offset by a decrease of $1,206,000 in Fellowships and Training Grants.

B) Neurological Disorders: The $812,000 decrease reflects an increase of $1,712,000 for research on epilepsy including the planned establishment of a comprehensive research center program; on multiple sclerosis, genetic and developmental disorders; further analysis of data from the collaborative perinatal project; and on virological and immunological aspects of chronic degenerative disease of the nervous system and a decrease of $2,524,000 for Training Grants.

C) Stroke and Nervous System Trauma: The $216,000 decrease reflects an increase of $354,000 for research on cerebrovascular disease and stroke, head injury and spinal cord injury, and nerve growth and regeneration and a decrease of $570,000 in Training Grants and Research Management and Program Services.

*Excludes 1973 appropriation restorations.

D) Fundamental Neurosciences: The increase of $95,000 reflects an increase of $237,000 to support the Institute's mission to elucidate the mechanisms responsible for normal function of the human nervous system and to understand the nature of its diseases and disorders and a decrease of $142,000 for Training Grants.

E) Intramural Laboratory and Clinical Research: The increase of $1,201,000 includes $246,000 built-in increase and $955,000 for increases in laboratory and clinical research programs to investigate the basic characteristics of the nervous system and its diseases.

F) Research Management and Program Services: The increase of $564,000 includes $247,000 for the NIH Mangement Fund, $84,000 for built-in increases, and $233,000 for additional program analysis, planning, and grant review functions.

Obligations by Object

	1974 Estimate	1975 Estimate	Increase or Decrease
Total number of permanent positions............................	520	520	-2
Full-time equivalent of all other positions............................	37	37	--
Average number of all employees.........	560	557	-3
Personnel compensation:			
Permanent positions..................	$ 8,705,000	$ 9,155,000	+$450,000
Positions other than permanent........	755,000	800,000	+45,000
Other personnel compensation..........	185,000	195,000	+10,000
Subtotal, personnel compensation.....	9,645,000	10,150,000	+505,000
Personnel benefits.....................	1,016,000	1,057,000	+41,000
Travel and transportation of persons....	410,000	435,000	+25,000
Transportation of things................	80,000	93,000	+13,000
Rent, communications and utilities......	482,000	531,000	+49,000
Printing and reproduction...............	208,000	234,000	+26,000
Other services:			
Project contracts.....................	10,145,000	9,787,000	-358,000
Payment to NIH Management Fund........	6,983,000	7,230,000	+247,000
Other................................	3,920,000	4,087,000	+167,000
Supplies and materials..................	1,241,000	1,302,000	+61,000
Equipment...............................	660,000	679,000	+19,000
Grants, subsidies and contributions.....	104,335,000	84,373,000	-19,962,000
Total obligations by object.........	139,125,000	119,958,000	-19,167,000
Total obligations excluding 1973 appropriation....................	119,993,000		

Significant Items in House and Senate Appropriations Committee Reports

Item	Action Taken or to be Taken
1974 House Report	
1. In order to maintain the regular research grant programs and the training grant and fellowship programs at the 1972 levels, the Committee added $18,875,000 to the estimate. The effect of these increases is to enable the Institute to fund the same number of new awards in 1974 as in 1972. (page 24 of the House Report)	1. The Institute has awarded new and competing projects in 1974 in an effort to bring the total amount up to the 1972 level.
1974 Senate Report	
1. The Committee, as a result of the inclusion of chiropractic services under Medicare, believes that an "independent unbiased" study be made of the fundamentals of the chiropractic profession. Accordingly a budget of as much as $2,000,000 should be earmarked for this study and chiropractic research, to be conducted by chiropractors. (page 49 of the Senate Report)	1. The Institute is convening a conference with national groups to evaluate the present status and future potential for chiropractic research.
2. The Committee has added additional funds for acute head and spinal cord injury research as well as research on the regeneration of the nervous system. The Committee believes that up to $4,500,000 of the increase provided by the Congress should be used for research in this area with special emphasis on research relating to the regeneration of the nervous system. (page 49 of the Senate Report)	2. Through research grants, contracts, and its intramural laboratory and clinical programs, the Institute has increased the research effort in this field. In 1974 two additional spinal cord acute injury research centers were established and it is planned to award another two in 1975. Major research included in these centers will be the evaluation of recent leads in central nervous system regeneration.

Item	
1974 Senate Report (cont'd)	
3. The Committee included additional funds to accelerate research on serious neurological and neuromuscular disorders with emphasis on multiple sclerosis and muscular disorders. (page 49 of the Senate Report)	3. The cause of many of the more serious neurological and neuromuscular disorders remains unknown. However, progress has been made in the diagnosis of muscular dystrophy and in the identification of genetic carriers. Also, significant improvement has recently evolved in the treatment of myasthenia gravis. A National Advisory Commission on Multiple Sclerosis was established last year and it issued its report to the Secretary, DHEW, in February, 1974.

Authorizing Legislation

	1975	
Legislation	Authorization	Appropriation Requested
Public Health Service Act Section 301--Research and Investigations in general	Indefinite	$119,958,000
Title IV, Part D--National Institute of Neurological Diseases and Blindness	Indefinite	
Public Law 90-639, Sec. 7--National Institute of Neurological Diseases and Stroke	Indefinite	

National Institute of Neurological Diseases and Stroke

Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
1965	$ 83,983,000	$ 83,264,000	$ 82,851,000	$ 82,851,000
1966	91,184,000	91,184,000	96,291,000	95,841,000
1967	100,171,000	105,008,000	110,008,000	110,008,000
1968	120,285,000	120,285,000	125,310,000	120,269,000
1969	123,765,000	119,244,000	125,244,000	121,504,500*
1970	97,667,000	95,438,000	106,187,000	101,547,000
1971	89,475,000	95,073,000	110,073,000	100,073,000
1972	91,015,000	103,454,000	133,454,000	111,445,000
1973	111,858,000	122,869,000	130,199,000	124,469,000**
1974	101,233,000	120,108,000	125,035,000	125,035,000***
1975	119,958,000			

* $21,519,000 transferred to National Eye Institute

** Note: This appropriation authority was the continuing resolution. The appropriation amount was the House Allowance, which was the lower of the House or Senate amounts in the first vetoed bill.

*** Appropriation after reduction, $119,993,000.

Justification

National Institute of Neurological Diseases and Stroke

	1974 Base*		1975 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits..........	520	$ 10,661,000	520	$ 11,207,000	--	+$546,000
Other expenses..........	--	109,332,000	--	108,751,000	--	-581,000
Total.............	520	119,993,000	520	119,958,000	--	-35,000

General Statement

Medical research at the National Institute of Neurological Diseases and Stroke is responsible for developing an increased understanding of the brain, spinal cord, and related nervous and sensory systems and the many disorders which afflict these areas. Many of these disorders interfere with mobility and often cause long-term disability such as that which occur in cerebral palsy, multiple sclerosis, muscular dystrophy and parkinsonism. Some interfere with education and employment such as epilepsy, deafness, and speech disorders. And one, stroke, is the third largest cause of death in this country and a major cause of serious disability.

These neurological and sensory disorders fall into 13 major program areas, each the subject of a specifically focused research effort. The research effort in these areas is carried out through extramural project research grants, center or program project research grants, intramural research projects, collaborative and field research projects and contract research projects. The program areas are as follows:

The neurological disorders of early life, includes cerebral palsy and such metabolic diseases as Tay-Sachs.

The neurological disorders of adult life including Parkinson's disease and Huntington's disease.

The cerebrovascular disorders, particularly stroke.

Epilepsy and related paroxysmal disorders including migraine headaches.

Multiple sclerosis and related disorders.

Neuromuscular disorders, particularly muscular dystrophy and myasthenia gravis.

Infectious diseases of the nervous system, including those chronic degenerative diseases caused by atypical and latent viruses.

Spinal cord and head injury, and nerve regeneration.

Tumors of the nervous system, particularly non-malignant brain tumors.

*Excludes 1973 appropriation restorations.

Neuroendocrine studies. This category includes studies on the autonomic nervous system, involving control of body temperature, bladder control, and respiration.

Neural aspects of learning and behavior. Studies of the nervous system in regard to sensory and motor behavior, perception, memory, learning, and locomotion.

Nervous system studies related to normal functions. These include the subcategories of anatomy, physiology and pharmacology in their applicability to normal functions. (For example, a study of the molecular structure of biological systems, or the metabolism of nervous and related structures.)

Sensory disorders include disorders of hearing and equilibrium, speech and language, and other higher CNS functions, and disorders of other senses.

DHEW - National Institutes of Health

CROSSWALK - 1974 COLUMN 1975 PRESIDENT'S BUDGET

INSTITUTE: National Institute of Neurological Diseases and Stroke

(amounts in thousands)

Mechanism / Program	Research Grants				Training Programs		Laboratory and Clinical Research	Research and Development Contracts	Other Direct Operations	Total
	Regular Program		Specials							
	Non-competing	Competing	Multi-disciplinary Centers	Other	Grants	Fellowships				
1974 Base Obligations										
1. Communicative Disorders	5,616	5,020	41	255	2,228	655		1,345	98	15,258
2. Neurological Disorders	18,065	15,900	1,709	1,239	4,682	2,273		5,738	6,631	56,237
3. Stroke & Nervous System Trauma	6,939	6,203	3,630	65	811	60		1,275	250	19,233
4. Fundamental Neurosciences	5,694	5,090	311	129	279	233		270	126	12,132
5. Intramural Lab and Clinical Research							7,032			7,032
6. Research Management & Program Services	154			152			4,837		4,958	10,101
Subtotal..........	36,468	32,213	5,691	1,840	8,000	3,221	11,869	8,628	12,063	119,993
Unobligated Balance Restored										
1. Commun. Disorders		1,980			1,364	10		218		3,572
2. Neurol. Disorders		4,995			3,262	30		848		9,135
3. Stroke & Nervous System Trauma		3,179			478			216		3,873
4. Fund. Neurosciences		1,377			217	10		235		1,839
5. Intramural Lab and Clinical Research							652			652
6. Research Management & Program Services									61	61
Subtotal...........		11,531			5,321	50	652	1,517	61	19,132
Total obligations........	36,468	43,744	5,691	1,840	13,321	3,271	12,521	10,145	12,124	139,125

DHEW - National Institutes of Health

CROSSWALK - 1975 COLUMN 1975 PRESIDENT'S BUDGET

INSTITUTE: National Institute of Neurological Diseases and Stroke

(amounts in thousands)

Mechanism	Research Grants									
	Regular Program		Specials		Training Programs		Laboratory and Clinical Research	Research and Development Contracts	Other Direct Operations	Total
Program	Non-competing	Competing	Multi-disciplinary Centers	Other	Grants	Fellowships				
1. Communicative Disorders	7,357	3,412	41	272	1,029	648		1,530	102	14,391
2. Neurological Disorders	23,492	10,890	1,709	1,314	2,158	2,432		6,510	6,920	55,425
3. Stroke and Nervous System Trauma	9,091	4,215	3,630	76	391	70		1,440	104	19,017
4. Fundamental Neurosciences	7,459	3,459	311	131	137	291		307	132	12,227
5. Intramural Lab and Clinical Research							8,233			8,233
6. Research Man. and Program Services	180			178			5,110		5,197	10,665
Total Obligations	47,579	21,976	5,691	1,971	3,715	3,441	13,343	9,787	12,455	119,958

National Institute of Neurological Diseases and Stroke
Budget Mechanism

	1974 Base*		1975 Estimate	
	Number	Amount	Number	Amount
Grants				
Regular				
Non-competing	622	36,468,000	721	47,579,000
Competing	377	21,884,000	300	16,826,000
New	232	9,035,000	220	3,900,000
Supplemental	(100)	1,294,000	(107)	1,250,000
Subtotal	1,231	68,681,000	1,241	69,555,000
Special				
Specialized Research Centers	--	5,691,000	--	5,691,000
Scientific Evaluation	--	152,000	--	178,000
Research Career Program	79	1,688,000	86	1,793,000
Subtotal	79	7,531,000	86	7,662,000
Total Grants	1,310	76,212,000	1,327	77,217,000
Fellowships				
Non-competing	18	221,000	201	3,009,000
Competing	--	--	--	--
New	200	3,000,000	29	432,000
Supplemental	--	--	--	--
Subtotal	218	3,221,000	230	3,441,000
Training Grants				
Non-competing	211	7,267,000	98	3,715,000
Competing	10	685,000	--	--
New	--	--	--	--
Supplemental	(4)	48,000	--	--
Subtotal	221	8,000,000	98	3,715,000
Laboratory & Clinical Research		11,869,000		13,343,000
Research & Development Contracts		8,628,000		9,787,000
Collaborative Research & Support		7,796,000		8,065,000
Biometry, Epidemiology, & Field Studies		--		--
International Center		--		--
Research Management & Program Services		4,267,000		4,390,000
TOTAL		119,993,000		119,958,000

*Excludes 1973 appropriation restorations.

Communicative Disorders

Authorizing Legislation: Public Health Service Act, Public Law 410,
Title IV, Part D

	1974 Base*		1975 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits..........	8	$ 52,000	8	$ 54,000	—	+$2,000
Other expenses..........	—	15,206,000	--	14,337,000	--	-869,000
Total..........	8	15,258,000	8	14,391,000	—	-867,000
Subactivities:						
Hearing and equilibrium	--	9,003,000	--	9,220,000	--	+217,000
Speech and language....	8	3,117,000	8	3,222,000	--	+105,000
Research training programs..............	—	3,138,000	--	1,949,000	--	-1,189,000
Total..........	8	15,258,000	8	14,391,000	--	-867,000
Funding mechanism:						
Research Grants						
Regular..............	—	10,636,000	—	10,769,000	—	+133,000
Special..............	--	296,000	—	313,000	—	+17,000
Subtotal..........	--	10,932,000	—	11,082,000	—	+150,000
Fellowships...........	--	655,000	—	648,000	—	-7,000
Training Grants.......	—	2,228,000	—	1,029,000	—	-1,199,000
Research and development contracts......	—	1,345,000	—	1,530,000	—	+185,000
Other Institute direct operations..........	8	98,000	8	102,000	--	+4,000
Total..........	8	15,258,000	8	14,391,000	—	-867,000

The Communicative Disorders program of the National Institute of Neurological Diseases and Stroke is concerned with research on improving the diagnosis, treatment, and prevention of diseases and disorders which affect the ear, nose and throat and hearing, language, and speech. Through study of diseases and the underlying neurologic mechanisms which are involved, the Institute is seeking to reduce the burdens imposed by these disorders on approximately 24 million persons in the country. The Institute's programs combine extramural research and training grants, intramural laboratory research, and contract-supported collaborative, clinical and applied research and are directed at improving understanding of the underlying functions involved in hearing, expressing ideas through speech, and in the central neural processing of language. They are also directed at learning how specific diseases interfere with these functions and at applying this understanding to the diagnosis, treatment, and prevention of these disorders.

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*Excludes 1973 appropriation restorations.

Objectives, 1975: In 1975, the Institute will seek, through a balanced program of clinical, basic and applied research, to exploit available opportunities for progress in advancing the diagnosis, treatment, and prevention of disorders and diseases of the ear, nose and throat and of human communication.

The Institute will continue to support clinical research in oto-rhinolaryngology and basic research in the communicative sciences and related fields through investigator-initiated research grant awards of the Extramural Program. Ongoing basic research in neurosciences relating to communicative disorders will continue in existing intramural laboratories and be augmented by the addition of the new Laboratory of Neuro-Otolaryngology (See Laboratory and Clinical Research also). Targeted research will continue through contract-directed clinical and applied research programs carried out by the Collaborative and Field Research Program.

The tables above reflect the distribution of resources to programs as well as the funding mechanisms used to support research in the communicative disorders.

Neurological Disorders

Authorizing Legislation: Public Health Service Act, Public Law 410,
Title IV, Part D

	1974 Base*		1975 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits..........	167	$ 3,488,000	167	$ 3,631,000	--	+$143,000
Other expenses..........	--	52,749,000	--	51,794,000	--	-955,000
Total...........	167	56,237,000	167	55,425,000	--	-812,000
Subactivities:						
Neurological disorders of early life..........	61	12,820,000	61	13,197,000	--	+377,000
Neurological disorders of adult life..........	10	3,408,000	10	3,473,000	--	+65,000
Epilepsy..............	8	5,692,000	8	6,000,000	--	+308,000
Sclerosing disorders..	23	3,892,000	23	4,035,000	--	+143,000
Neuromuscular disorders	3	6,165,000	3	6,203,000	--	+38,000
Infectious diseases of the central nervous system..............	58	4,045,000	58	4,382,000	--	+337,000
Tumors of the nervous system.............	3	1,159,000	3	1,249,000	--	+90,000
Neuroendocrine studies	--	3,545,000	--	3,585,000	--	+40,000
Learning and behavior	1	1,814,000	1	1,825,000	--	+11,000
Other sensory disorders	--	5,503,000	--	5,572,000	--	+69,000
Research training	--	8,194,000	--	5,904,000	--	-2,290,000
Total...........	167	56,237,000	167	55,425,000	--	-812,000
Budget mechanism:						
Research Grants:						
Regular.............	--	33,965,000	--	34,382,000	--	+417,000
Special.............	--	2,948,000	--	3,023,000	--	+75,000
Subtotal..........	--	36,913,000	--	37,405,000	--	+492,000
Fellowships.........	--	2,273,000	--	2,432,000	--	+159,000
Training grants.....	--	4,682,000	--	2,158,000	--	-2,524,000
Research and development contracts.........	--	5,738,000	--	6,510,000	--	+772,000
Other Institute direct operations........	167	6,631,000	167	6,920,000	--	+289,000
Total...........	167	56,237,000	167	55,425,000	--	-812,000

*Excludes 1973 appropriation restorations.

Of the four major research program segments, Neurological Disorders contains the largest grouping of subprograms. These neurological diseases and disorders fall into ten separate areas, each the subject of a specifically focused research effort directed at advancing knowledge of the human nervous system and how it functions in health and disease.

Objectives, 1975: Research emphasis in 1975 will be focued on: epilepsy including the initiation of the pilot phase in the establishment of a comprehensive epilepsy research center program; on multiple sclerosis; genetic and developmental disorders; on the further analysis of data collected from the collaborative perinatal project; and on virological and immunological aspects of chronic degenerative diseases of the nervous system. Significant research being conducted in some of the program areas include the following:

a. Neurological Disorders of Early Life: This category includes the Collaborative Perinatal Project. This program is nearing completion after a long-term follow-up at seven and at eight years of age on children born to 50,000 women at 12 collaborating major medical centers.

The basic objective of the program is to relate complications, conditions, and events that occur during a woman's pregnancy or during her labor and delivery, to subsequent abnormalities exhibited by the child of the pregnancy.

As data collection nears its end, the major emphasis of the program is shifting to data analysis and the publication of reports on the Project's research findings.

The analysis will cover 10 primary areas: cerebral palsy and motor disorders; mental retardation; vision abnormalities; convulsive disorders; learning disorders and minimal brain dysfunction; communicative disorders (problems of speech, language, and hearing); congenital malformations; multiple problems associated with low birth-weight and gestational age (prematurity); and the children who died during the interval of the Study, with particular emphasis on the abnormalities found in the central nervous system.

b. Epilepsy: Part of the 1974 increase will be used to initiate a pilot program towards the establishment of comprehensive research and treatment centers for epilepsy and related convulsive disorders which are not now in existence in this country. These centers will stress a comprehensive approach to applied and fundamental research, and will be strongly oriented toward the development of new and improved methods of diagnosis, treatment, and rehabilitation regardless of age or severity. The primary emphasis will be on the application of new research findings to humans, with basic research supporting the primary goals as required. The ultimate goals of these centers will be the development of new antiepileptic drugs in the search for complete control of seizures, the reduction of the debilitating side effects of presently available epileptic drugs, and restoration of patients with controlled seizures to a useful and productive life.

c. Multiple Sclerosis: The Institute is conducting and supporting approximately 65 research projects related to MS in the attempt to discover the cause of multiple sclerosis. Half of these projects are in biochemistry and neurochemistry, and the others relate to immunology, neurophysiology, pathology, viruses, and clinical studies. Chemical and metabolic characteristics of normal and abnormal myelin have been widely investigated in an attempt to reach an understanding of how myelin is formed, maintained and degraded in the normal nervous system. The search for a viral agent is closely related to this approach, since many investigators believe that an auto-immune process may be triggered by a virus in the causation of multiple sclerosis.

Two large NINDS-supported clinical projects are conducting studies on patients, involving immunological, virological, and neurochemical aspects relevant to demyelinating disease.

On October 25, 1972, Congress enacted Public Law 92-563 to establish a 9-member National Advisory Commission on Multiple Sclerosis to determine the most effective means of finding the cause of and cures and treatments for multiple sclerosis. The Commission in 1974 completed a comprehensive review of the status of MS research which highlights areas of promise. The final report will be published before the end of fiscal year 1974.

d. Muscular Dystrophy, Myasthenia Gravis and other Neuromuscular Diseases: Research in this group of diseases is centered in the Institute's Medical Neurology Branch. NINDS also supports over 140 research grants which are seeking to clarify the causes, disease processes and treatment of this complex group of conditions. Recently the introduction of a new treatment for myasthenia gravis by an Institute scientist with high-single-dose alternate-day Prednisone promises to be the treatment of choice in many of these patients. Improved methods of treatment of hypokalemic periodic paralysis is another significant advance. Other research findings are gradually increasing our knowledge of the pathological processes and the causes of this heterogeneous group of diseases.

e. Infectious Diseases of the Central Nervous System: The Institute's program in slow and atypical viruses as described in the Section on Laboratory and Clinical Research is a major research undertaking. In addition, the Institute has a highly significant program carried on by its Infectious Disease Branch in relation to the Collaborative Perinatal Research project. This program is concerned with the study of the relationship between viral, bacterial, mycoplasma and protazoal infections in the perinatal period, and resultant birth defects and pediatric neurological diseases. Recent advances have been made in studies of the effects of herpes virus infections, toxoplasmosis, cytomegalovirus infections and rubella vaccine during pregnancy. The role of measles virus in the causation of subacute sclerosing pan-encephalitis, a fatal disease in children, has been clarified. Studies are also in progress on the relationship of myxovirus-like viruses in the etiology of multiple sclerosis to briefly outline activities in research on the infectious diseases and their effects on the Central Nervous System.

f. Brain tumors: Brain tumors comprise a group of several histologically and biologically different tumors. Brain tumors of childhood represent 26% of childhood cancers, but are quite different from the brain tumors of adults which constitute only about 7% of adult cancer. Nearly one-half of the people who die of neurological disease other than stroke die of brain tumors.

Surgical removal of the encapsulated well-differentiated slow-growing tumors can effect a cure, and the development of microsurgical techniques is increasing the number of surgical cures. The malignant brain tumors of adults, the glioblastoma multiforme, which are about 45% of adult brain tumors have a median survival of about 5 months. Recent work in the Branch of Surgical Neurology has shown that when combined oral and intratumoral chemotherapy are added to conventional therapy, surgery and X-Ray, the mean survival time is doubled when compared to controls receiving conventional treatment only. In addition it has been shown that the cellular immune mechanisms of patients with low grade gliomas (benign course) are the same as in patients without tumors and cancer, but the high grade glioma patients (malignant course) display decreased cellular immune responses.

Stroke and Nervous System Trauma

Authorizing Legislation: Public Health Service Act, Public Law 410,
Title IV, Part D

	1974 Base*		1975 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits........	6	$ 131,000	6	$ 137,000	--	+$6,000
Other expenses........	--	19,102,000	--	18,880,000	--	-222,000
Total..........	6	19,233,000	6	19,017,000	--	-216,000
Subactivities:						
Stroke..............	3	10,278,000	3	10,376,000	--	+98,000
Trauma and injury...	3	8,019,000	3	8,104,000	--	+85,000
Research training...	--	936,000	--	537,000	--	-399,000
Total..........	6	19,233,000	6	19,017,000	--	-216,000
Budget mechanism:						
Research Grants						
Regular..........	--	13,142,000	--	13,306,000	--	+164,000
Special..........	--	3,695,000	--	3,706,000	--	+11,000
Subtotal........	--	16,837,000	--	17,012,000	--	+175,000
Fellowships.........	--	60,000	--	70,000	--	+10,000
Training Grants.....	--	811,000	--	391,000	--	-420,000
Research and development contracts..	--	1,275,000	--	1,440,000	--	+165,000
Other Institute direct operations.	6	250,000	6	104,000	--	-146,000
Total..........	6	19,233,000	6	19,017,000	--	-216,000

Research under this program is directed towards cerebrovascular disease and stroke, head injury and spinal cord injury, and nerve growth and regeneration.

Objectives, 1975: The funds requested for 1975 will be used to continue the research carried on in 1973 and 1974. Emphasis will be on the following:

> Stroke - Research programs on stroke during 1975 will be directed towards five main problems; primary prevention, secondary prevention, basic research, acute care, and rehabilitation.

*Excludes 1973 appropriation restorations.

Spinal Cord Injury and Regeneration - Plans in 1975 include the establishment of two additional spinal cord acute injury research centers, and the evaluation of recent leads in central nerve regeneration.

Head Injury - Electrical monitoring of cerebral reflex activity in unconscious patients after stimulation offers considerable promise as a non-invasive quantitative measure of viability of damaged brain tissue. The accuracy and usefulness of such measurements in establishing prognosis for survival and, in later stages, for recovery of function requires further testing.

The specific research accomplishments in 1973 and 1974 for these programs are as follows:

Stroke - Basic research has shown that nervous as well as chemical control mechanisms regulate blood flow to injured brain tissue, and at best can only be modified by specific drugs. Currently, intensive study is in progress in animal models to identify the crucial factors determining the prevention or reversibility of the stroke process. Important aspects are studies in microcirculation of brain areas with special attention to its local regulation, on oxygen lack and edema, and the roles of transmitter amines.

In 1973 there were ten stroke acute care research units established and support will continue in 1974. These research units function as institution focal points for increased attention to the development and improvement of methods for prevention, diagnosis and monitoring of the acute stroke, development and evaluation of treatment methods and training of professional and scientific personnel in this research area.

There is controversy over the definition and diagnosis of transient ischemic attack (little strokes). A prospective study is now underway with contract support to give a descriptive definition of transient ischemic attack. This study is based on its frequency in hospital admissions and the character of the attacks. In order to obtain similar generalized information and particularly in an older age group, a project is planned to obtain information by means of self-administered questionnaires by elderly persons in retirement communities.

Spinal Cord Injury and Nerve Growth and Regeneration - Three spinal cord acute injury research centers were established in 1973 and one more was funded in 1974. These centers will concentrate on immediate damage to the injured spinal cord and improved methods of treatment. Research findings suggest that if the acute injury is properly treated immediately, permanent damage may be prevented or minimized. Therefore, the development of improved methods of treatment of the acute injury in its early stages is of great importance.

Research in the treatment of spinal cord injury has recently received an impetus due to improved understanding of the basic pathophysiological mechanisms set in motion by the injury. Another area of promise is in nerve regeneration as a result of the recent demonstration of terminal and collateral regeneration in axons of the central nervous system. Because of these findings, the Institute has created a new section on Nerve Degeneration and Regeneration in its Laboratory of Neurochemistry and plans to expand its research effort in 1974 by exploring the promising new leads in this field.

(This effort is budgeted under Intramural Research.) In addition, an NANDS Council Subcommittee has been formed to conduct a comprehensive review of the status of research on central nerve regeneration and to highlight areas of promise.

Head Injury - Development in several regions within the country of helicopter ambulance services and highly specialized acute head injury treatment centers has reduced local mortality rates from the more severe types of head injury. However, emergency diagnostic methods have been invasive, each bearing certain risks of further complications in the natural evolution of brain injury.

The Institute's research program in head injury is carried out through research grants, clinical research centers, intramural projects, and contracts. There are currently three clinical research centers which provide firm bases for the important combination of clinical material, laboratory facilities, and experienced researchers.

In the collaborative area, the Institute has begun a study of the patterns of recovery of psychological function in head injured patients. While great enthusiasm has developed within the national and local community for emergency care facilities, helicopter ambulance services and intensive care units for acute accident victims, little research activity has focused on the quality of recovery among survivors, and because of this collaborative contract-supported research is being developed in this area. One of the high priorities in 1974 is the development and field testing of a standardized diagnostic classification of head and spinal injuries and a standardized graded morbidity scale for use in longitudinal studies in humans.

All of these programs will receive additional support in 1974 and 1975 as a result of specific Congressional increases in 1974. Increases of up to $4,500,000 were provided for research in the above programs with special emphasis on research relating to the regeneration of the nervous system.

A new program to be funded in this area is chiropractic research. The Congress in 1974 directed that as much as $2,000,000 should be used for this study. As a result, the Institute is convening a conference with national groups to evaluate the present status and future potential for chiropractic research.

Fundamental Neurosciences

Authorizing Legislation: Public Health Service Act, Public Law 410, Title IV, Part D.

	1974 Base*		1975 Estimate		Increase of Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits..........	6	$ 66,000	6	$ 69,000	--	+$3,000
Other Expenses..........	--	12,066,000	--	12,158,000	--	+92,000
Total........	6	12,132,000	6	12,227,000	--	+95,000
Subactivities:						
Nervous System Studies related to normal function............	--	6,535,000	--	6,613,000	--	+78,000
Multicategorical......	6	4,956,000	6	5,055,000	--	+99,000
Research Training.....	--	641,000	--	559,000	--	-82,000
Total........	6	12,132,000	6	12,227,000	--	+95,000
Budget Mechanism:						
Research Grants:						
Regular.............	--	10,784,000	--	10,918,000	--	+134,000
Special.............	--	440,000	--	442,000	--	+2,000
Subtotal..........	--	11,224,000	--	11,360,000	--	+136,000
Fellowships...........	--	233,000	--	291,000	--	+58,000
Training Grants.......	--	279,000	--	137,000	--	-142,000
Research & Development Contracts...........	--	270,000	--	307,000	--	+37,000
Other Institute direct operations..........	6	126,000	--	132,000	--	+6,000
Total........	6	12,132,000	6	12,227,000	--	+95,000

Support of research in the fundamental neurosciences is basic to the Institute's mission to elucidate the mechanisms responsible for normal function of the human nervous system and to understand the nature of its diseases and disorders. There is a vital continuum from the discoveries of the laboratory scientists to their application to disease and health problems by the clinician.

In 1975, the amount requested to continue support of research in the fundamental neurosciences is $12,227,000. These funds will be used to support research grants in ongoing projects, the nature and extent of which is briefly outlined below, and to start new highly meritorious scientific projects. It is to be noted, however, that this amount does not include those funds requested for the support of such research in the Institute's Intramural Program (which is detailed separately in the following section on Laboratory and Clinical Research).

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*Excludes 1973 appropriation restorations.

Part of the research in the fundamental neurosciences is carried on in the Institute's Intramural Branches and Laboratories. The major portion of research support, however, is supplied to the biomedical community through research grants. Among these individual research grants funded by NINDS a number of significant and intriguing studies are in progress: the role of nerve growth factor in spinal cord regeneration; synaptic plasticity; isolation of receptor proteins; seizures and retardation of brain growth; cerebellar locus for dilantin action; the valium group of drugs as anticonvulsants; correlation of the recurrence rate of seizures (highest recurrence for multiple seizure types); immunological approaches to possible antiglial factors in multiple sclerosis and antineuronal factors in amyotrophic lateral sclerosis; ischemic lesions in stroke and in cord and head injuries; electroencephalographic changes often the earliest sign of slow virus infection; comparative studies of virally-induced demyelination (progressive multifocal leucoencephalopathy, canine distemper, mouse hepatitis, visna in sheep); reproduction in animals of myasthenia gravis after injection of antibodies to muscle receptor protein and alleviation with neostigmine; evaluation of damage by constant noise to the cochlea; vestibular function in Meniere's disease; diagnostic applications of electroacoustic impedance; role of trace metals in mechanisms of olfaction and taste.

This brief account of the scope of the NINDS support to the Fundamental Neurosciences is necessarily incomplete. In summary, the most elementary problem of neurosciences, the conduction of the nerve impulse seems to be slowly yielding under the applications of increasingly powerful concepts and techniques. On the other hand, the neurosciences is the constant collaborator of the clinical neurologist because the ultimate solutions and the ultimate challenges are in the human central nervous system where the highest levels of functioning characterize memory, learning, communication and behavior, and the complexities of their aberrations.

Intramural Laboratory and Clinical Research

Authorizing Legislation: Public Health Service Act, Public Law 410,
Title IV, Part D

	1974 Base*		1975 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits..........	242	$5,193,000	242	$5,396,000	--	+$203,000
Other expenses..........	--	1,839,000	--	2,837,000	--	+998,000
Total...........	242	7,032,000	242	8,233,000	--	+1,201,000

The intramural research activities of the Institute are directed toward a broad program to investigate the basic characteristics of the nervous system and its diseases. Supporting this program effort are four branches and nine laboratories. The following are in the Clinical Research area; Medical Neurology, Surgical Neurology, Developmental and Metabolic Neurology and Electroencephalography. Under the Laboratory Research area are: Biophysics, Neurochemistry, Neurophysiology, Molecular Biology, Experimental Neurology, Neural Control, Neuropathology and Neuroanatomical Sciences, Perinatal Physiology, and Central Nervous System Studies.

Objectives, 1975: All phases of the Intramural research program will be actively pursued in 1975 in addition to the programs highlighted below. Many of the laboratories and branches not specifically mentioned for the purposes of this document have highly productive programs in progress with evidence of promising research. The accomplishments and breakthroughs are:

a. Genetically-determined lipid storage diseases. The culmination of 15 years of fundamental research on the metabolism of sphingoglycolipids has been the elucidation of the biochemical defects in the group of genetically-determined lipodystrophies or lipid storage diseases (e.g., Gaucher's, Niemann-Pick and Tay-Sachs diseases) afflicting mostly children and almost uniformly fatal. NINDS intramural scientists discovered that the defect in each case is a lack of a key enzyme in the degradative pathway for the specific lipid that accumulates in each disorder. On the basis of this knowledge, simple specific tests have been devised to diagnose suspected cases, to identify carriers, and to monitor pregnancies at risk by examining cells in amniotic fluid obtained by amniocentesis and hence provide genetic counselling for the parents. Now efforts are being directed toward two goals: the first is the isolation and complete purification of the involved enzymes as a prelude to ascertaining the molecular nature of the genetic defect; and the second is the development of procedures for possible replacement therapy either by direct administration of the missing enzyme or by resort to various alternatives, such as injection of the missing enzyme enclosed within permeable microspheres or bonding of the missing enzyme to a supporting matrix over which the patient's blood could be passed (in an analogy to renal dialysis). These are truly pioneering studies.

*Excludes 1973 appropriation restorations

b. The slow viruses. The culmination of another long-term study by NINDS intramural scientists has been the discovery that a number of the degenerative diseases of the human nervous system are slow or atypical virus infections manifested many years after initial contact with the virus. This NINDS research was the first to demonstrate that chronic degenerative diseases of man could be caused by such slow or atypical virus infections. Such infections include a group of presenile dementias. Other slow virus infections of the human brain involve common viruses like measles virus (the cause of SSPE, subacute sclerosing panencephalitis) that remain masked for very long periods of time and then produce relentless subacute or chronic pathology of the brain or papova viruses that produce tumors in experimental animals yet in the human brain cause demyelination (as in PML, progressive multifocal leucoencephalopathy).

These discoveries by NINDS intramural scientists and grantees raise some very fundamental questions. How many other chronic, degenerative disorders of the nervous system may be caused by slow viruses? Could these agents be major factors in aging (senescence) of the nervous system? Could these agents be the cause of multiple sclerosis, amyotrophic lateral sclerosis and the like? These studies represent some of the most significant and provocative programs within the NINDS.

c. Laboratory of Neuro-Otolaryngology. An important development in 1974 was the creation of a laboratory of neuro-otolaryngology to strengthen the Institute's research in diseases of the ear and the central nervous system pathways of hearing, vestibular disorders, and the central processes of the brain involved in language development and speech production. The creation of this laboratory will ultimately allow the Institute to develop a unique multidisciplinary approach to solving complex problems which are gap areas in our knowledge, and which have long needed an intensified research effort. The coordination of effort needed by a number of scientific disciplines would be extremely difficult to attain in any biomedical research setting in the country other than at the National Institutes of Health.

d. Neuro-Immunology. It is now apparent from the important accomplishments of the Institute's slow virus and other infecious diseases research programs that coordination is needed among the programs especially with the development of a new direction to the research effort in immunology. The application of the latest techniques and knowledge of cellular immune systems will be of exceptional importance to the furtherance of these projects. The development of this effort is actively underway and is expected to be accomplished in late FY 1974 or in early FY 1975.

e. General. Although many of the accomplishments have been dealt with in detail elsewhere it is considered pertinent to list some again to demonstrate the importance of support to research in the neurosciences. A rich yield of stimulating and important findings has emerged from intramural projects during FY 1974: solubilization and characterization of the Na-K-ATPase enzyme that promise elucidation of mechanisms responsible for the conversion of cellular energy into the transport of sodium, potassium, and calcium across neural membranes; role of astrocytes in the fluid and ionic balance in brain tissues; dynamics of brain edema after ischemic insults; techniques for observing myelination *in vivo*; roles of immune response and genetic histo-compatibility in axonal regeneration; transmembrane transport activity as an indicator of cell differentiation; characteristics of isolated sodium-specific channel in artificial lipid membranes; development of a variety of special electrode devices for neural control prosthesis; elucidation of sensory (visual) input mechanisms and of the rhythmicity of pacemaker neurons; developmental shifts in seizure propagation from subcortical to cortical loci; isolation of apparently specific glyco-proteins from glial tumors; evaluation of spinal cord circulation by radioisotope angiography; circulatory insufficiency mechanisms underlying Duchenne's muscular dystrophy; prednisone therapy for myasthenia and myotonia; fluorimetric monitoring _in situ_ of energy changes in cerebral cortex during seizures; isolation and therapeutic trials of the respective degradative enzymes genetically deleted from tissues in Fabry's, Gaucher's and Tay-Sachs' diseases; demonstration of the slow viral transmission of the hereditary form of Creutzfeld-Jakob disease; suggestive evidence for a slow virus cause for Alzheimer's disease and for some forms of multiple sclerosis; and partial purification and successful concentration of atypical slow virus agents (kuru, scrapie, etc.) preliminary to detailed characterization.

Research Management and Program Services

Authorizing Legislation: Public Health Service Act, Public Law 410,
Title IV, Part D

	1974 Base*		1975 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits..........	91	$ 1,731,000	91	$ 1,920,000	--	+$189,000
Other expenses..........	--	8,370,000	--	8,745,000	--	+375,000
Total..........	91	10,101,000	91	10,665,000	--	+564,000

Included in this activity is the administrative support required for the Extramural Programs and the Office of the Director. The Extramural Programs administers the Institute's grant and award programs in support of medical research and training in the neurological and communicative disorders. The Office of the Director provides the professional and administrative direction of the Institute's activities. Also included in this program are funds to support program evaluation.

Objectives, 1975: The Institute will maintain the same level of administrative support as furnished in 1973 and 1974 with emphasis on the refinement of the extramural reporting system and the manpower reporting system within the Office of the Director.

*Excludes 1973 appropriation restorations

NATIONAL INSTITUTES OF HEALTH

National Institute of Neurological Diseases and Stroke

Program Purpose and Accomplishments

Activity: Communicative Disorders (Speech and Hearing) [Public Health Service Act, Public Law 410, Title IV, Part D]

1974			1975	
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
8	$15,258,000	Indefinite	8	$14,391,000

Purpose: The Communicative Disorders program of the National Institute of Neurological Diseases and Stroke is concerned with research on improving the diagnosis, treatment, and prevention of diseases and disorders which affect the ear, and hearing, language and speech.

Explanation: The Institute's programs combine extramural research and training grants, intramural laboratory research, and contract-supported collaborative, clinical and applied research and are directed at improving understanding of the underlying functions involved in hearing, expressing ideas through speech, and in the central neural processing of language.

Accomplishments in 1974: In 1974, under this program 161 research grants, 45 fellowships, 62 training grants, and 14 contracts were awarded. The Institute's programs in 1974 were directed towards improving understanding of the underlying functions involved in hearing, expressing ideas through speech, and in the central neural processing of language. Also, programs were directed at learning how specific diseases interfere with these functions and at applying this understanding to the diagnosis, treatment, and prevention of these disorders.

Objectives for 1975: The estimate for 1975 provides for 163 research grants, 45 fellowships, 25 training grants, and 16 research contracts. The Institute will continue to support clinical research in oto-rhinolaryngology and basic research in the communicative sciences and related fields through investigator-initiated research grant awards of the Extramural Program. Ongoing basic research in neurosciences relating to communicative disorders will continue in existing intramural laboratories.

NATIONAL INSTITUTES OF HEALTH

National Institute of Neurological Diseases and Stroke

Program Purpose and Accomplishments

Activity: Neurological Disorders (Public Health Service Act, Public Law 410, Title IV, Part D)

1974			1975	
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
167	$56,237,000	Indefinite	167	$55,425,000

Purpose: Of the four major research program segments, this one contains the largest grouping of subprograms. These neurological diseases fall into ten separate areas, each subject of a specifically focused research effort and directed at significantly advancing knowledge of the human nervous system and of how it functions in health and disease.

Explanation: Research support is directed towards neurological diseases of epilepsy, brain tumors, muscular disorders, multiple sclerosis, neurological diseases of childhood, minimal brain dysfunction, neurological aspects of learning and behavior, slow viruses, and Parkinson's disease.

Accomplishments in 1974: In 1974, 728 research grants, 153 fellowships, 122 training grants, and 54 contracts were awarded. Research was directed towards all the neurological disorders with emphasis in the fields of epilepsy, sclerosing disorders, parkinsonism and infectious diseases of the central nervous system.

Objectives for 1975: The estimate for 1975 provides for 732 research grants, 162 fellowships, 55 training grants and 57 contracts. Research emphasis in 1975 will be focused on: epilepsy including continuation of the pilot phase for the establishment of a comprehensive program centered on research and treatment of epilepsy; on multiple sclerosis; genetic and developmental disorders; on the further analysis of data collected from the collaborative perinatal project; and on virological and immunological aspects of infectious disorders.

NATIONAL INSTITUTES OF HEALTH

National Institute of Neurological Diseases and Stroke

Program Purpose and Accomplishments

Activity: Stroke, Nervous System Trauma (Public Health Service Act, Public Law 410, Title IV, Part D)

1974		1975		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
6	$19,233,000	Indefinite	6	$19,017,000

Purpose: Research under this program is directed towards cerebrovascular disease and stroke, head injury, spinal cord injury, and nerve growth and regeneration.

Explanation: This program includes the establishment of clinical research centers, acute spinal cord injury centers, and stroke acute care research units.

Accomplishments in 1974: In 1974, support was provided for 153 research grants, 4 fellowships, 25 training grants, and 18 contracts. Research was directed towards stroke, head injury, spinal cord injury, and nerve growth and regeneration.

Objectives for 1975: The estimate for 1975 provides for 155 research grants, 5 fellowships, 12 training grants, and 19 contracts. Research programs on stroke during 1975 will be directed towards five main problems; primary prevention, secondary prevention, basic research, acute care, and rehabilitation. In the fields of spinal cord injury and regeneration, plans include the establishment of two additional spinal cord acute injury research centers, and the evaluation of recent leads in central nervous system regeneration.

NATIONAL INSTITUTES OF HEALTH

National Institute of Neurological Diseases and Stroke

Program Purpose and Accomplishments

Activity: Fundamental Neurosciences (Public Health Service Act, Public Law 410, Title IV, Part D)

1974		1975		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
6	$12,132,000	Indefinite	6	$12,227,000

Purpose: Support of research in the fundamental neurosciences is basic to the Institute's mission to elucidate the mechanisms responsible for normal functioning of the human nervous system and to understand the nature of its diseases and disorders.

Explanation: This program supports research grants in ongoing projects and starts new highly meritorious scientific projects, such as nervous system studies related to normal function including anatomy, physiology, and pharmacology.

Accomplishments in 1974: In 1974, 189 research grants, 16 fellowships, 12 training grants, and 2 contracts were awarded. Research was directed towards the mechanisms responsible for normal functioning of the human nervous system and to the understanding of the nature of its diseases and disorders.

Objectives in 1975: The estimate for 1975 provides for 191 research grants, 18 fellowships, 6 training grants, and 2 contracts. The amount requested is for continued support of research in the fundamental neurosciences. These funds will be used to support research grants in ongoing projects, and to start new highly meritorious scientific projects, such as nervous system studies related to normal function including anatomy, physiology, and pharmacology.

NATIONAL INSTITUTES OF HEALTH

National Institute of Neurological Diseases and Stroke

Program Purpose and Accomplishments

Activity: Intramural Laboratory and Clinical Research (Public Health Service Act, Public Law 410, Title IV, Part D)

1974		1975		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
242	$7,032,000	Indefinite	242	$8,233,000

Purpose: The intramural research activities of the Institute are directed toward a broad program to investigate the basic characteristics of the nervous system and its diseases.

Explanation: Supporting this program effort are four branches and nine laboratories. The following are in the Clinical Research area: Medical Neurology, Surgical Neurology, Developmental and Metabolic Neurology, and Electroencephalography. Under the Laboratory Research area are: Biophysics, Neurochemistry, Neurophysiology, Molecular Biology, Experimental Neurology, Neural Control, Neuropathology and Neuroanatomical Sciences, Perinatal Physiology, and Central Nervous System Studies.

Accomplishments in 1974: In 1974 the Institute established a laboratory of neuro-otology. This program focuses on improving the basic understanding of the physiological, biophysical and psychological mechanisms involved in the reception and interpretation of sound as well as the vocalization of speech.

Objectives for 1975: In 1975 the Institute will continue basic and clinical research in neurological and communicative disorders including both ongoing and new projects. These projects will include research in the field of cerebral trauma, particularly head injury. Emphasis will also be given to the experimental production of head injury in primates and in formulating mathematical models of whiplash injury. Also, research in the field of muscular disorders, epilepsy, parkinsonism, and genetic disorders will be conducted.

NATIONAL INSTITUTES OF HEALTH

National Institute of Neurological Diseases and Stroke

Program Purpose and Accomplishments

Activity: Research Management and Program Services (Public Health Service Act, Public Law 410, Title IV, Part D)

1974		1975		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
91	$10,101,000	Indefinite	91	$10,665,000

Purpose: Included in this activity is the administrative support required for the Extramural Programs and the Office of the Director. The Extramural Programs administers the Institute's grant and award programs in support of medical research and training in the neurological and communicative disorders.

Explanation: The Office of the Director provides the professional and administrative direction of the Institute's activities. Also included in this program are funds to support program evaluation.

Accomplishments in 1974: Management's expanding need for access to multiplex data and its comprehensive analysis to provide a firm base for program planning, evaluating and reporting, demands a fully automated information system capable of being adjusted to changing requirements. Such a system has been established and will permit a more refined assessment of Institute support patterns and needs in research and research training in neurological and communicative disorders.

Objectives for 1975: The Institute will maintain the same level of administrative support as furnished in 1974 with emphasis on the refinement of the extramural reporting system and the manpower reporting system within the Office of the Director.

Thursday, March 28, 1974.

NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

WITNESSES

DR. DORLAND J. DAVIS, DIRECTOR

DR. ROBERT S. STONE, DIRECTOR, NATIONAL INSTITUTES OF HEALTH

DR. DeWITT STETTEN, JR., DEPUTY DIRECTOR FOR SCIENCE, NATIONAL INSTITUTES OF HEALTH

DR. JOHN R. SEAL, SCIENTIFIC DIRECTOR, NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

WALTER H. MAGRUDER, EXECUTIVE OFFICER, NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

MARTIN J. FULLER, JR., FINANCIAL MANAGEMENT OFFICER, NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

LEON M. SCHWARTZ, ASSOCIATE DIRECTOR FOR ADMINISTRATION, NATIONAL INSTITUTES OF HEALTH

LELAND B. MAY, ACTING DIRECTOR OF FINANCIAL MANAGEMENT, NATIONAL INSTITUTES OF HEALTH

CHARLES MILLER, DEPUTY ASSISTANT DIRECTOR, BUDGET

Object Classification (in thousands of dollars)

Identification code 09-25-0885-0-1-651		1973 actual	1974 est.	1975 est.
	Direct obligations:			
	Personnel compensation:			
11.1	Permanent positions	8,914	9,215	9,477
11.3	Positions other than permanent	310	315	315
11.5	Other personnel compensation	412	425	425
	Total personnel compensation	9,636	9,955	10,217
12.1	Personnel benefits: Civilian	1,333	1,377	1,413
21.0	Travel and transportation of persons	386	425	450
22.0	Transportation of things	77	95	95
23.0	Rent, communications, and utilities	366	450	500
24.0	Printing and reproduction	76	105	105
25.0	Other services	18,799	21,815	23,803
26.0	Supplies and materials	2,231	2,700	3,072
31.0	Equipment	569	680	730
41.0	Grants, subsidies, and contributions	69,553	83,175	70,019
	Total direct obligations	103,026	120,777	110,404
	Reimbursable obligations:			
	Personnel compensation:			
11.1	Permanent positions	31	30	---------
11.3	Positions other than permanent	1	---------	---------
11.5	Other personnel compensation	6	2	---------
	Total personnel compensation	38	32	---------
12.1	Personnel benefits: Civilian	11	3	---------
21.0	Travel and transportation of persons	13	15	10
22.0	Transportation of things	31	35	35
24.0	Printing and reproduction	---------	1	1
25.0	Other services	137	279	259
26.0	Supplies and materials	42	45	45
31.0	Equipment	48	50	50
42.0	Insurance claims and indemnities	1	---------	---------
	Total reimbursable obligations	321	460	400
99.0	Total obligations	103,347	121,237	100,804

Personnel Summary

Total number of permanent positions	635	598	596
Full-time equivalent of other positions	46	50	50
Average paid employment	669	665	649
Average GS grade	8.5	8.6	8.6
Average GS salary	$14,260	$15,138	$15,473
Average salary of ungraded positions	$11,138	$12,018	$12,253

Program and Financing (in thousands of dollars)

	Identification code 09-25-0885-0-1-651	1973 actual	1974 est.	1975 est.
	Program by activities:			
	Direct program:			
	1. Allergic and immunologic diseases	26,770	30,832	27,218
	2. Bacterial and fungal diseases	24,089	28,572	23,992
	3. Viral diseases	22,220	24,134	21,888
	4. Parasitic diseases	9,886	10,798	9,782
	5. Intramural laboratory and clinical research	18,765	20,479	21,562
	6. Research management and program services	4,785	5,962	5,962
	Total direct program	106,515	120,777	110,404
	Reimbursable program:			
	5. Intramural laboratory and clinical research	321	460	400
	Total program costs, funded [1]	106,836	121,237	110,804
	Change in selected resources (undelivered orders)	−3,489		
10	Total obligations	103,347	121,237	110,804
	Financing:			
11	Receipts and reimbursements from: Federal funds	−321	−460	−400
25	Unobligated balance lapsing	10,408		
	Unobligated balance restored		−10,408	
	Budget authority	**113,434**	**110,369**	**110,404**
	Budget authority:			
40	Appropriation	113,414	114,000	110,404
	Withheld from obligation and expenditure (Public Law 93-192)		−3,596	
41	Transferred to other accounts		−35	
42	Transferred from other accounts	20		
43	**Appropriation (adjusted)**	**113,434**	**110,369**	**110,404**
	Relation of obligations to outlays:			
71	Obligations incurred, net	103,026	120,777	110,404
72	Obligated balance, start of year	63,842	60,763	61,974
74	Obligated balance, end of year	−60,763	−61,974	−50,528
77	Adjustments in expired accounts	289		
90	Outlays	106,394	119,566	121,850

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[1] Includes capital outlay as follows: 1973, $810 thousand; 1974, $680 thousand; 1975, $730 thousand.

NOTES

Includes $178 thousand in 1975 for activities previously financed from (in thousands of dollars):

	1973	*1974*
National institute of General Medical Sciences	150	150
Departmental management	2	2

Excludes $60 thousand in 1975 for activities transferred to: Office of Assistant Secretary for Health. Comparable amounts for 1973 ($60 thousand) and 1974 ($60 thousand) are included above.

Excludes $35 thousand in 1974 and 1975 for activities transferred to Departmental Management. Comparable amount for 1973 ($35 thousand) is included above.

WITNESS INTRODUCTION

Mr. FLOOD. We have the National Institute of Allergy and Infectious Diseases, the presentation to be made by Dr. Dorland J. Davis, Director.

We will insert your biographical sketch in the record, Doctor.

[The sketch follows:]

BIOGRAPHICAL SKETCH

Name: Dorland J. Davis, M.D.

Position: Director, National Institute of Allergy and Infectious Diseases.

Birthplace and date: Chicago, Ill., July 2, 1911.

Education: B.S., University of Illinois, 1933; M.D., Johns Hopkins University, 1937; Dr. P.H. (epidemiology), Johns Hopkins University, 1940; Certified by the American Board of Preventive Medicine and Public Health, 1949.

Experience: Director, National Institute of Allergy and Infectious Diseases, National Institutes of Health, 1964 to present; Associate Director, National Institute of Allergy and Infectious Diseases, National Institutes of Health, 1956–64; Chief, Laboratory of Infectious Diseases, National Microbiological Institute (now National Institute of Allergy and Infectious Diseases) NIH, 1954–56; Commissioned Officer on duty at National Institutes of Health (1943–44 on duty in North Africa for the State Department) advanced through grades to Assistant Surgeon General (1968), 1939 to present.

Association memberships: Fellow, American Academy of Microbiology; Fellow, American College of Preventive Medicine; Fellow, American Academy of Allergy; American Association of Immunologists; American Epidemiological Society; American Society of Tropical Medicine and Hygiene; Board of Directors, Gorgas Memorial Institute of Tropical and Preventive Medicine, Inc.; Member National Research Council, Division of Medical Sciences (Executive Committee, 1966–71).

Special awards, citations, or publications: Edward Rhodes Stitt Award, Association of Military Surgeons of the United States, 1955; Meritorious Service Medal, 1967, of the Commissioned Corps, USPHS; Distinguished Service Medal, 1971, of the Commissioned Corps, USPHS; Publication of 48 papers on infectious diseases.

Mr. FLOOD. Have you anybody with you that you would like to introduce to us?

Dr. DAVIS. I have Mr. Walter Magruder, on my left, the executive officer.

Behind me are Dr. John Seal, Scientific Director, and Mr. Martin Fuller, financial management officer of the Institute.

Mr. FLOOD. How do you wish to proceed with your statement, Doctor?

Dr. DAVIS. I will be glad to read it, Mr. Chairman.

Mr. FLOOD. You may proceed.

OPENING STATEMENT

Dr. DAVIS. Mr. Chairman and members of the committee, infectious diseases continue to have an enormous impact on our Nation's health. In spite of antibiotics, these illnesses are alarmingly far from being conquered.

For example, each year about 1.5 million patients develop hospital-acquired diseases which prolong hospitalization and directly contribute to the spiraling cost of medical care. In fact, public health officials conservatively estimate that these illnesses cost the Nation nearly $750 million annually.

Other reports indicate that an estimated 51 million cases of influenza and 30,000 deaths were attributed to the Hong Kong flu epidemic in the United States. This epidemic of 1968–69 cost us $2.5 billions for medical care alone. Also, during the 1964 rubella epidemic, approximately 20,000 children were born with congenital disease resulting in an economic loss to the Nation estimated at $1.5 billion. Fortunately, the rubella vaccine—licensed in 1969 after extensive NIAID-supported field trials—averted another epidemic which had been expected in the early 1970's.

Facts such as these have led one authority to predict that improvement in our ability to prevent common infectious diseases would be more likely to upgrade the adequacy of medical care than would the development of new drugs and treatment methods. He also has stated that, if costs of medical care are to be reduced, prevention of disease offers the only prospect of success.

Our Institute is keenly aware of the benefits of preventing infectious diseases. Cost-effective analyses have been reported to the Congress in recent years on poliomyelitis, measles, and tuberculosis. The NIAID has developed research strategies with overall goals to reduce the tolls caused by other infectious diseases. The strategies, of course, are dynamic. And as I focus on some of the most recent exciting research activities, you should recognize that the nature of our approach depends to some degree upon what information we already have about a disease, coupled with the opportunities and talent for further pursuit.

HEPATITIS

After decades of discouragement it looks as if we are on the right track for finding the causes of viral hepatitis—the first step toward disease prevention.

First, in late 1973, three of our own NIAID scientists, using a technique called immune electronmicroscopy, visualized the virus that causes infectious hepatitis, known as hepatitis A. This discovery and the development of a technique with which to detect antibody to this hepatitis A virus now provides a means of distinguishing hepatitis A from the other form of the disease—hepatitis B. It should lead to the development of simpler tests for diagnosing the infectious form of the disease. Immune electronmicroscopy may also prove valuable in standardizing the potency of immune serum globulin, a disease-fighting blood substance which is used to protect close contacts of hepatitis A patients.

Also, in late 1973, a team of NIAID-supported scientists found good evidence concerning the causative agent of hepatitis B—sometimes referred to as serum hepatitis because it usually can be traced to inoculation of blood or blood products from infected individuals. These investigators detected in the inner core of a so-called Dane particle an enzyme that directs the manufacturing of genetic material. This discovery of enzyme activity offers proof that the Dane particle is actually a virus, and, from other evidence, almost surely the virus of hepatitis B. The enzyme is already serving as a marker of infection, since scientists have detected it in the serum of patients in the early stages of illness.

To insure a well-coordinated research attack within the DHEW, a Hepatitis Policy Liaison Committee has been established. This committee coordinates research activities conducted by NIAID, the

National Heart and Lung Institute, and the Food and Drug Administration—the three DHEW groups currently having major contract programs.

INFLUENZA AND PNEUMONIA VACCINES

Last year, I spoke about our efforts to avert or diminish the consequences of the next influence pandemic—expected in the late 1970's. Our need is to produce an effective influenza vaccine quickly after a major change in the structure of the influenza virus is discovered. Historically, these major changes occur about every 10 years. When they occur, immunity to influenza—acquired either by a case of the flu or vaccination—is no longer protective and whole populations once again become susceptible to the new strain.

To help meet this need, NIAID intramural scientists are developing a prototype vaccine. In the new preparation, the influenza virus is altered to produce mutants that grow only at the cooler temperatures of the upper respiratory tract where they cause little disease. At the same time, the mutants protect against serious infection of the lungs. Our scientists have been able to transfer this temperature-sensitive trait from one influenza strain to another by deliberately mating, or cross-breeding, two viruses. In a similar fashion they could quite possibly transfer a fast-growing trait from an older virus to a newly emerging pandemic strain, thereby shortening the time it takes to produce a new live vaccine.

Other scientists supported by NIAID are developing a vaccine against one of the two proteins on the surface of the influenza virus. Theoretically, this vaccine would not prevent infection, but it should diminish viral growth in the cells to the extent that actual disease would not develop. Later, when exposed to the natural virus, a vaccine would develop high levels of protective antibody and achieve full immunity without developing symptoms of influenza. This experimental vaccine is currently being tested in Texas to determine the proper dosage and the level of antibody response associated with it.

Taken together, influenza and pneumonia ranked fourth among diseases causing deaths in 1972. Since an estimated 25,000 to 40,000 of these deaths are caused by pneumococcal pneumonia, the Institute established a program several years ago to develop a pneumococcal pneumonia vaccine. NIAID surveillance studies have confirmed that high risk populations include the American Indians, the chronically ill, and those individuals whose respiratory tracts had been weakened by viral infections, such as influenza. Three candidate vaccines have been evaluated for safety and their ability to produce antibodies, and clinical field trials are underway in North Carolina and California. We should have results on the value of these vaccines in 2 years.

Mr. Patten. I am taking a trip, so I just got a couple of shots for the flu. Is this the same experiment?

Dr. Davis. No, sir. The vaccine which you received is not an experimental vaccine. It is one of the standard vaccines which is approved by the Bureau of Biologics of the Food and Drug Administration.

Mr. Patten. I just wondered whether you were using us for guinea pigs.

DIARRHEAL DISEASES

Dr. DAVIS. For several years, scientists supported and sponsored by our Institute have been studying epidemics of Asiatic chlora, a devastating form of bacterial diarrhea. They have now demonstrated the effectiveness of an easily prepared salt solution, given by mouth, for treatment in areas with primitive medical facilities.

More recently, the Institute has supported the development of a new chlora vaccine to replace the current one, which is only protective for 3 to 6 months. We plan to test this vaccine in large-scale field trials in Bangladesh, where the disease occurs nearly every year. Experience gathered in handling epidemics of Asiatic cholera is now being applied to treatment and prevention of acute diarrhea in certain American Indian infants.

Recently, an NIAID team discovered viruses infecting the parasites that cause the human diarrheal disease known as amebic dysentery. These scientists are now trying to determine if the viruses cause variations of intensity in the disease. This discovery, which represents the first time viruses have ever been found in ameba, will also provide a simple, one-cell animal model system in which to study viral mechanisms.

VENEREAL DISEASE

Three years ago, our Institute was convinced that we needed new research approaches to reduce the incidence of venereal disease. Therefore, we established a special grants program to encourage research on the bacteria causing VD and their interaction with man. The level of our VD research funding has increased from $128,000 in fiscal year 1971 to a proposed level of $2.2 millions for fiscal year 1975.

One exciting research advance in this area concerns a promising blood screening test for gonorrhea developed by NIAID grantees. The procedure involves analyzing blood samples for the presence of antibodies to pili, the hairlike appendages present only on the cell walls of the disease-producing gonococci. The test is particularly valuable in detecting gonorrhea in asymptomatic women who give negative readings on routine bacterial cultures. These women are the most serious reservoir for the spread of gonorrhea. Apparently, the test is not as effective in asymptomatic men.

A Wisconsin grantee has developed another potentially valuable diagnostic tool which should aid public health officials interested in tracing the chain of infection at the community level. Called auxotyping, it provides a practical method of classifying gonococci according to their growth in different media. It also can be used by physicians to distinguish between those patients who are truly penicillin-treatment failures and those who have actually been reinfected by a different auxotype during an interval between treatments.

A grantee from Utah has been studying the interaction between the gonococci and leukocytes—the human white blood cells which help protect the body against disease. He has found that the gonococci behave quite differently from other types of bacteria with regard to these interactions. These findings may help us understand man's seeming lack of immunity to repeated gonococcal infections.

IMMUNOLOGY RESEARCH

Until recently, the general public has thought of immunity and immunology in terms of a vaccine that prevents smallpox or a case of mumps that provides a person with immunity to a second infection. Immunology is much more than that. It is concerned with the complex protective mechanisms of the body and how they work under normal and abnormal conditions. In the past 20 years, discoveries in immunology—including immunologic diagnostic techniques and therapy—have pervaded most areas of medicine.

During the past decade, our Institute has been one of the leading forces in applying principles of immunology to organ transplantation. We have supported the development of tissue matching and immunosuppressive agents to counteract the rejection phenomena everpresent with organ transplants, as described in the attached special report. Advances in this field account for the increase in kidney transplants alone from about 200 a year in the United States in 1964 to an estimated 3,000 in 1973.

On a smaller scale, we have been interested in tumor immunology. BCG, an antituberculosis vaccine, has been shown effective in treating some tumors of animals. An NIAID biophysicist who has developed a unique instrument for making a better vaccine from the cell walls of the TB bacteria, has purified isolated components of the BCG cell walls, and in collaboration with the National Cancer Institute scientists, explored their role in tumor immunity. In preliminary studies, it appears that these components are more active than BCG in tumor regression or prevention and may have a significant impact on the immunotherapy of cancer in man.

ASTHMA AND ALLERGIC DISEASE CENTERS

Actually, an allergy is an exaggerated immune response. In the last 15 years, scientists have learned much about the mechanisms of the immune response, including the discovery of IgE—the skin-sensitizing antibody that combines with foreign antigens and leads to allergic reactions. This accumulation of knowledge led the Institute in 1971 to establish a program of Asthma and Allergic Disease Centers. We now have 17 centers located in 13 States, and propose to allocate $1.6 millions in primary support to these Centers in fiscal year 1975.

A new ragweed extract being evaluated at one Center may improve hay fever therapy. It contains a specially prepared version of an important protein in ragweed pollen. Preliminary studies reveal that the new preparation is at least as effective as the current extract used in allergy shots and that it might produce fewer side effects. A research laboratory procedure from Sweden called RAST—the acronym for radioallergosorbent technique—is proving to be reliable in diagnosing allergy and evaluating immunotherapy. It quite possibly could become the tool for standardizing allergenic extracts used for allergy testing and desensitization. A physician at one Center has already used RAST to measure the potency of 11 allergenic extracts of short ragweed pollen and found substantial differences.

Until recently, extracts used to desensitize persons highly allergic to insect stings were made from the body of whole insects. Now, studies from two Centers suggest that each insect species has its own specific allergenic substance contained within the insect's venom. In documented bee sting cases, treatment with the venom extract has been successful after treatment with whole bee extract failed.

Scientists at several of these Centers have participated over the years in evaluation trials of a new type of asthma drug, disodium cromoglycate, which was licensed by the FDA last summer. This drug is now being prescribed for selected asthmatics to prevent attacks, and is helpful in reducing some patients' dependence on steroid drugs. This is particularly important in treating children whose growth may be affected through prolonged use of steroids.

These are some of the developments indicating progress in the battle against infectious diseases and allergies.

In conclusion, Mr. Chairman, the 1975 request for the National Institute of Allergy and Infectious Diseases is $110,404,000. I shall be pleased to try to answer any questions and supply additional information desired for the record.

1975 BUDGET REQUEST

Mr. Flood. Your 1975 budget request for the National Institute of Allergy and Infectious Diseases is at the same level as the 1974 adjusted appropriation of $110,404,000; is that right?

Dr. Davis. Yes, sir.

Mr. Flood. This budget also provides for a reduction of about $5 million in your regular and special grant programs. How come? Why is that?

Dr. Davis. Mr. Chairman, I think if you look on page 266 and page 267, in the right-hand column, it shows in comparison of those two that the amount of funds devoted to each of the program areas, namely, allergic, bacterial, viral, and parasitic disease, is essentially the same in both years. The differences in the reduction of the research grants are offset by several factors.

One is the increase in total fellowships over 1974, which is shown on page 267 at the bottom of the fellowship column, a $2 million increase.

There is a $1 million increase in the laboratory and clinical research, which is almost mandatory.

Mr. Flood. You show the same thing on page 268, do you not?

Dr. Davis. Yes. That gives similar figures.

Mr. Flood. Those are the figures you are working from.

Dr. Davis. There is also an increase in the amount of funds devoted to research and development contracts.

Mr. Flood. The reduction from $66 million to $61 million is where you get the minus $5 million?

Dr. Davis. That is correct. These are offset by increases in the fellowships, in the laboratory and clinical research, and in research and development contracts.

RESTORED FUNDS

Mr. Flood. In 1974, you received $10.4 million of the restored 1973 funds.

Mr. Davis. That is right.

Mr. Flood. How did you spend that money? That is, in which areas of the Institute did you put those funds?

Dr. Davis. This is shown on page 266.

Mr. Flood. We have the same problem with all the Institutes. You are not the only one. I am going to ask you again about multiyear grant awards. We are asking you the same thing. In which areas of your Institute did you spend this money?

Dr. Davis. It was about equally divided between research grants, training programs, and R. & D. contracts, as shown on page 266, in the next to the bottom line.

MULTIYEAR FUNDING

Mr. Flood. Did you make any of these multiyear grant awards, 2 years or more?

Dr. Davis. Yes, we did. Out of 1974 funds; none out of 1973 funds.

Mr. Flood. We want for the record a revision of that table appearing on page 268 of your justifications. Specifically, we want to see in the 1974 column these restored funds, and in the 1975 column, the impact of the action taken in 1974.

Of course, at the same time, be sure that you include fiscal year 1972 and fiscal year 1973 in that table.

Also for the record, we want a table for fiscal years 1972, 1973, 1974, and 1975, showing how much you invested in each of the program areas.

[The information follows:]

NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

Obligations by Budget Mechanism Showing "True" Program Levels in 1974 - 1975

(Amounts in thousands)

Budget Mechanism	1972 No.	1972 Amount	1973 No.	1973 Amount	1974 No.	1974 Amount	1975 No.	1975 Amount
Grants								
Regular								
Noncompeting	767	$38,086	744	$41,667	820	$43,166	819	$48,252
Competing	184	9,973	133	7,541	146	8,168	84	5,262
New	175	7,211	146	7,034	157	7,842	108	6,830
Supplemental	(7)	128	(16)	279	(19)	354	(15)	280
Subtotal	1,126	55,398	1,023	56,521	1,123	59,530	1,011	60,624
Special								
Scientific evaluation	---	150	---	150	---	150	---	176
International ctr. for med. res.	4	2,399	4	2,399	4	2,399	4	2,399
Research career program	109	2,647	80	2,009	81	2,035	93	2,319
Subtotal	113	5,196	84	4,558	85	4,584	97	4,894
Total Grants	1,239	60,594	1,107	61,079	1,208	64,114	1,108	65,518
Fellowships								
Noncompeting	65	650	27	232	12	95	136	2,327
Competing	2	20	--	---	--	--	--	---
New	28	262	14	155	210	3,129	137	2,760
Supplemental	--	--	--	--	--	---	--	---
Subtotal	95	932	41	387	222	3,224	273	5,087
Training Grants								
Noncompeting	120	7,311	125	6,224	79	4,524	63	5,001
Competing	12	902	1	62	6	100	--	---
New	14	617	2	58	1	20	--	---
Supplemental	(9)	92	(6)	38	--	1,781	--	---
Subtotal	146	8,922	128	6,382	86	6,425	63	5,001
Laboratory and clinical research	--	18,753	--	18,633	--	20,479	--	21,562
Research and development contracts	124	10,228	122	9,846	136	11,842	136	12,336
Res. mgmt. and program services	--	4,616	--	4,781	--	5,904	--	5,962
Grand total	--	104,045	--	101,108	--	111,988	--	115,466

NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

Obligations by Budget Activity Showing "True" Program Levels in 1974 - 1975

(Amounts in thousands)

Budget Program	1973		1974		1975	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Allergic and immunologic diseases	---	$25,032	---	$28,012	---	$28,711
Bacterial and fungal diseases	---	22,581	---	25,145	---	25,867
Viral diseases	---	20,830	---	22,211	---	23,021
Parasitic diseases	---	9,251	---	10,237	---	10,343
Intramural laboratory and clinical research	509	18,633	479	20,479	479	21,562
Research management and program services	122	4,781	117	5,904	117	5,962
Total	631	101,108	596	111,988	596	115,466

NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

Distribution of 1973
Impounded Funds
(Amounts in thousands)

Budget Mechanism	No. of Awards	Amount	Remarks
Research Grants	11	$541	Allergic & Immunologic Diseases
	14	711	Bacterial & Fungal Diseases
	6	312	Viral Diseases
	6	179	Parasitic Diseases
Fellowships	41	459	Allergic & Immunologic Diseases
	36	400	Bacterial & Fungal Diseases
	28	305	Viral Diseases
	2	19	Parasitic Diseases
Training Grants	1	641	Allergic & Immunologic Diseases
	4	1,118	Bacterial & Fungal Diseases
	2	820	Viral Diseases
	-	22	Parasitic Diseases
Research & Development Contracts	2	106	Allergic & Immunologic Diseases
	8	850	Bacterial & Fungal Diseases
	2	106	Viral Diseases
Total	163	6,589	

NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

Multi-year Funding from 1974 Appropriation

(Amounts in thousands)

Budget Mechanism	No. of Awards	Total Amount	Amount Affecting 1975 Funding	Remarks
Research Grants	28	$2,691	$1,319	Allergic & Immunologic Diseases
	30	2,741	1,343	Bacterial & Fungal Diseases
	16	1,960	960	Viral Diseases
	9	636	312	Parasitic Diseases
Fellowships	9	274	134	Allergic & Immunologic Diseases
	8	240	118	Bacterial & Fungal Diseases
	7	210	103	Viral Diseases
	5	150	73	Parasitic Diseases
Training Grants	1	81	40	Allergic & Immunologic Diseases
	8	841	414	Bacterial & Fungal Diseases
	2	143	70	Viral Diseases
	4	359	176	Parasitic Diseases
Total	127	10,326	5,062	

NEW RESEARCH GRANTS

Mr. FLOOD. How many new research grants will you make with the 1975 budget request?

Dr. DAVIS. The estimate is that we will make about 192 new and competing grants.

Mr. FLOOD. In which program areas will you make these awards?

Dr. DAVIS. We expect they will be distributed essentially the way they are in 1974. Most of them will be in allergy and infectious diseases, and the fewest number will be in parasitic diseases.

Mr. FLOOD. Be sure when you put this together you do not fall on your face on this one. There are the tables. I look at the tables and they are great. They answer all the questions. It shows all the grants and all the areas.

Then I ask in which program areas will the new awards be made? That is a wrap-up question. I just asked you about the 1975 program. You told me. Now I want to know in what program areas will the money go for 1975?

Dr. DAVIS. We have some detailed information here on the program.

Mr. FLOOD. In what program areas?

Dr. DAVIS. In allergic and immunologic diseases, we expect to make 67 new competing awards.

Mr. FLOOD. You do not have to give me the numbers now. I want to know in what areas.

Dr. DAVIS. The four program areas are: (1) allergic and immunologic diseases; (2) bacterial and diarrheal diseases, where we will have 61 program awards; (3) the viral diseases, where we propose 37; and (4) parasitic diseases, in which we propose 27.

INFLUENZA RESEARCH

Mr. FLOOD. Every year we discuss the subject of influenza research, first, because we are very much interested in the subject and, second, because we are getting a lot of letters from physicians, which is a new thing, and, of course, from other interested parties, complaining that not enough is being done in this area.

In view of that, can you tell us what is your Institute doing to eliminate this costly infectious disease?

Dr. DAVIS. First, Mr. Chairman, we have increased our funding for influenza and respiratory diseases from 1973 at $2.7 million, by $1 million for the next year, $3.7 million.

There is a great deal of work going on trying to develop new vaccines for influenza. I am speaking specifically about the virus disease influenza, which is a distinct clinical entity.

There are 4 general lines of investigation.

One, there are the temperature-sensitive mutants about which I spoke last year.

There is another one which is being developed by one of our grantees in New York, the recombinants, that is, mating various strains of influenza virus to combine the desirable protective effects with the ability to grow rapidly so vaccines can be produced quickly.

There are some studies going on at the University of Michigan with another type of vaccine which is called the cold adapted mutants.

Then there is another type of vaccine which I mentioned previously, known as the antineurominidase vaccine, which acts against one of the proteins in the strain.

These are going ahead vigorously. Our program is increasing.

I should mention that we have just had an exchange visit by some of our staff and grantees with Russian scientists in Russia to try to get some new ideas on the way the Russians deal with their problem. They have a very serious problem of influenza and respiratory disease in Russia, apparently even worse than we have in this country.

We are moving in a number of different areas. The new vaccines as they are produced are being tested in different selected populations for their antigenicity and duration of protection.

NEW APPROACH TO CONTROL OF INFLUENZA

Mr. Flood. As you know, a new approach to the prevention and control of influenza has been proposed by a leading virologist at the Mt. Sinai School of Medicine in New York. You know about that?

Dr. Davis. Yes.

Mr. Flood. Can you tell us more about this approach and what are the chances of its reducing the size or nature of the influenza epidemic?

Dr. Davis. This is a very promising approach. The scientist is Dr. Edwin Kilbourne, who is one of our grantees and has been for some time. His idea is to vaccinate against one of the two major proteins on the coat of the influenza virus. When a person vaccinated with that antigen is exposed to the whole, complete virus, then he becomes fully protected.

It is a very novel approach.

Mr. Flood. Some of our people took a look at this. I saw a story when I was back in the district, in the Wilkes-Barre Times-Leader for February 7, the caption of which was: "New Approach to Prevention of Flu Seen." Subtitle: "Study Will Be Made on 2,000 Elementary Pupils."

It is an AP story out of New York. It has to do with Dr. Kilbourne. I see this quotation:

> Dr. Edwin D. Kilbourne said the idea is to achieve "a lesser victory" against the disease by limiting the degree of the infection while at the same time allowing enough infection so the person builds up a long-range immunity to the influenza virus.

That may sound all right to you, but that will scare you know what out of the average person who reads it.

Will you explain why this is a very practical thing?

Dr. Davis. The hope is that this would provide, for one thing, a more effective immunity, one that is longer lasting, and one that is simpler and easier to prepare.

The final answer, of course, will be obtained only when we do get the results of the trials.

TOTAL FOR RESPIRATORY DISEASES

Mr. Flood. How much of your 1975 budget will be spent on influenza and, of course, other respiratory disease research? We cannot have flu run the whole show. How much will we spend, not only on flu, but the other respiratory research as well?

Dr. Davis. Our estimate for the total amount for influenza and respiratory diseases for 1975 is $3,710,000. Of that, about $2,500,000 will be spent on influenza. This is an increase over previous years.

[The following material was supplied for the record:]

ACUTE RESPIRATORY DISEASE

Acute respiratory disease remains a problem of great concern to public health officials. It accounted for over 55 percent of all reported acute disease in the United States in 1972. Suffering due to respiratory infections, combined with their economic cost of $4.8 billions in time lost from work, represents a heavy burden for the American people.

Knowledge about control and treatment of acute respiratory diseases is incomplete. Licensed vaccines are available to protect partially against only one -- influenza. Antibiotics can be used to treat some bacterial infections, such as pneumococcal pneumonia and meningococcal meningitis, or infections caused by mycoplasma, but there are virtually no drugs to treat the vast majority of acute respiratory infections caused by viruses.

Research is under way to meet the urgent need for new or improved vaccines. Scientists are conducting field trials on vaccines against a number of bacterial infections, as well as smaller clinical evaluations of several promising candidates for improved influenza vaccines. In earlier stages of investigation are vaccines for viral and bacterial respiratory infections such as parainfluenza virus and streptococcal infections.

Many of these studies are supported by the National Institute of Allergy and Infectious Diseases under its coordinated research effort. Intramural research is conducted in the Institute's laboratories in Bethesda, Maryland; research grants support investigations at universities and medical institutions throughout the country; and collaborative studies are carried out through research contracts and interagency agreements. Other government agencies with related interests in acute respiratory disease are the Center for Disease Control, Food and Drug Administration, Department of Defense, and Department of Agriculture.

Obligations for programs in Acute Respiratory Disease

	1971	1972	1973	1974 estimate	1975 estimate
National Institutes of Health:					
National Institute of Allergy and Infectious Diseases..........	$5,765,000	$6,305,000	$6,691,000	$6,870,000	$7,100,000

NATIONAL INSTITUTES OF HEALTH

National Institute of Allergy and Infectious Diseases

Influenza Vaccines

The Problem. The first influenza vaccine was licensed in 1945, but the disease has not yet been conquered. Nearly 30 years later, in 1972, it was estimated by the National Center for Health Statistics that more than 102 million cases of influenza had occurred in the United States during that year. Although 40 million Americans comprise the group at greatest risk of developing complications after influenza infection -- those for whom the vaccine is specifically recommended -- only about fifteen million doses of vaccine are produced each year, and not all of these doses reach the high risk group.

In the past, this inadequate use of influenza vaccines has been attributed to low levels of efficacy and numerous side effects. Today, however, current influenza A vaccines are believed to be about 80 percent effective, and purification efforts in recent years have reduced side effects significantly.

The principal factor still contributing to the vaccine's limited effectiveness is the influenza virus's unique ability to change periodically, undergoing minor changes almost every season and a major modification every 10 to 12 years. When this happens, immunity to influenza -- acquired by a bout of flu or a vaccine -- is no longer protective and whole populations once again become susceptible to the new strain.

When a major change takes place, influenza occurs in a world-wide epidemic or pandemic. The last pandemic in 1968 -- the well-known Hong Kong flu -- caused more than 90 million cases of flu in the U.S. during the six months of the peak period and resulted in an estimated 25,000 to 30,000 excess deaths. A pandemic of similar severity is predicted for the late 1970's.

The Attack. In preparation for this expected pandemic, the National Institute of Allergy and Infectious Diseases has expanded its attack on influenza in all program areas. Intramurally, research aimed at improving understanding of the influenza virus itself, as well as at developing better vaccines, is continuing. Grants for extramural influenza studies cover topics from basic investigations into the structure of the virus to vaccine development. Within the collaborative program, a special effort specifically targeted against influenza was established this year on the recommendation of the Influenza Steering Group. This Group, composed of government and non-government scientists, was appointed in 1971 to assist in devising research strategies for the pandemic. The Group has held several scientific workshops, including two in 1973, and has been instrumental in indicating additional areas where research is needed.

Traditionally, killed influenza virus vaccines have been used to control outbreaks of influenza. For some time, however, many scientists have felt that a weakened or attenuated live virus vaccine, given by nasal spray or nose drops, would be more effective than the present method. Not only are smaller doses of a live vaccine needed to confer immunity, but nasal application of a live vaccine would expose the respiratory tract directly to a weakened version of the flu virus. Since the upper respiratory tract has its own local system of immunity, production of antibodies (protective substances) would be most effectively stimulated there.

Live Vaccines. For any influenza vaccine to be more effective, ways must be found to update it quickly whenever a new strain of virus emerges. NIAID scientists believe they are close to solving this problem with a technique they developed for tailoring the virus used in vaccines to meet current changes in the so-called wild virus.

The propensity of the influenza virus to change periodically is believed due to the ability of the virus to undergo recombination, in which one strain of virus can exchange genes with another and produce a new or modified strain. Some years ago, Dr. Edwin Kilbourne, an NIAID grantee at Mount Sinai School of Medicine in New York, suggested that by taking advantage of this ability of the flu virus, scientists could, in theory, have a virus "bank" from which they could draw parent strains and tailor-make vaccines to counteract current epidemics.

Dr. Kilbourne and NIAID scientists have been moving toward this goal. First, Dr. Robert Chanock, Dr. Brian Murphy and their co-workers at NIAID altered the genes of a strain of influenza virus to produce so-called "temperature-sensitive (ts)" mutants. Such a ts mutant virus grows only in the cooler nasal passages and throat, not in the lungs. This infection produces little illness but seems to stimulate production of local protective antibodies. At the same time, Dr. Kilbourne and his group deliberately mated two or more influenza viruses with desired traits and inactivated the offspring. The resulting recombinant vaccine, known as X-31, was tested successfully in a large group of military trainees in 1971.

In 1972, Dr. Chanock, Dr. Murphy and their group developed a prototype vaccine that uses the ideas behind both ts mutants and recombinants. They combined the ts mutant of the older 1965 influenza virus with the Hong Kong 1968 virus. The ease with which the altered gene of the 1965 virus was transferred to the Hong Kong strain led scientists to believe that it should be possible to make a similar transfer of a defective gene (the ts gene, for instance) to any new virus when it emerged. Using recombinant techniques, scientists might also be able to transfer to the new virus a fast-growing trait from an older virus. This would shorten the time it takes to produce a new vaccine and would make it available in time to thwart an impending epidemic.

The prototype vaccine of Dr. Chanock's, prepared by Flow Laboratories (a contractor of NIAID), is now being tested in various populations (including normal adults, adults at high risk, and children) by several other NIAID contractors at the University of Virginia, University of Rochester, and Washington, D. C., Children's Hospital. Preliminary results are promising.

The appearance of the new London strain of the influenza virus during the winter of 1972-1973 gave investigators a chance to apply the ts mutant and recombinant techniques to development of a vaccine for the "London flu." Problems encountered in choosing a recombined virus which would stimulate an adequate antibody response without causing disease is now leading to further work on the genetics of the ts mutants. Dr. Chanock is attempting to find biological methods for determining which ts mutant progeny of the cross of a wild virus and a ts mutant will cause infection and immunity but no illness. Under contract, biochemical studies of the genetics of ts mutants will be performed in order to understand where the mutation occurs and how to transfer it without affecting the antigenicity (immunity-stimulating) properties of the virus.

Neuraminidase-specific Vaccines. A second approach to live virus vaccines using the recombinant technique alone is of interest to NIAID contractors. Scientists know that there are two antigens, proteins which stimulate the production of antibodies, on the surface of influenza viruses. These are known as hemagglutinin and neuraminidase.

Dr. Kilbourne first mated the London flu virus with a fast growing virus and produced a recombinant he called X-37. He then recombined the X-37 with an equine flu strain. The resulting X-38 vaccine has the antigenic neuraminidase of the London flu and the irrelevant hemagglutinin of the equine virus. The equine hemagglutinin is irrelevant because antibody to it will not protect against a human flu virus. Dr. Robert Couch, an NIAID contractor at Baylor University School of Medicine in Houston, is now testing the X-38 vaccine to determine the proper dosage and the level of antibody response associated with it. People given such a neuraminidase-specific vaccine are not actually protected against the disease until they encounter the virus naturally. At that time, they will not become ill or transmit the disease to others, but will develop immunity to further infection with that virus.

Subunit Vaccines. Presently available influenza vaccines tend to cause systemic reactions in children, so NIAID-supported scientists and others are now investigating the pediatric use of purified subunit vaccines. There are many antigenic components in the influenza virus -- neuraminidase, hemagglutinin, the outer protein coat, and others. Investigators, working under contract, are about to initiate studies to determine whether a subunit -- a single antigenic component obtained by breaking apart the virus -- can be gathered in quantity, purified, pertinent antigens recombined, and used safely to stimulate antibody in children.

Dr. Charles Phillips, an NIAID Research Career Development Awardee, was a member of a group at the University of Vermont College of Medicine who recently evaluated killed disrupted influenza virus particle vaccine in children. The vaccine containing both the Hong Kong strain of the influenza A_2 virus and an influenza B virus was given to 33 children. It proved to be both antigenic and well-tolerated in the children indicating the feasibility of the purified subunit approach.

How Mutation Occurs. While such research on vaccines will aid present efforts to control influenza, more knowledge about the nature of the pandemic viruses is needed. An important question still unanswered is whether these new viruses arise by mutation from existing human strains or by recombination of human viruses with genetic traits from animal or bird strains. Dr. Robert Webster, an NIAID grantee at St. Jude Children's Research Hospital in Memphis, studied the Asian and Hong Kong strains of influenza A_2 virus and found no similarity between the hemagglutinin subunits of the two strains. This suggests that the Hong Kong virus's hemagglutinin did not result from the mutation of an earlier A_2 virus.

Dr. Webster then expanded these studies to compare the biochemical structure of the hemagglutinin antigens of the Hong Kong strain with those of a duck and an equine influenza virus. While one portion of the hemagglutinin subunit of each of the three viruses showed several differences, another part of the hemagglutinin was almost identical, suggesting genetic recombination.

Using mammalian and poultry influenza A viruses, Dr. Webster and his group then infected two groups each of turkeys and pigs. Uninfected birds and animals were found to be infected following natural exposure to infected subjects, and recombinant viruses were recovered from tissue samples of both turkeys and pigs. Thus, for the first time, genetic recombination of influenza A virus was demonstrated in a living host under simulated conditions of natural transmission. However, since natural transmission of the recombinant viruses did not take place, the scientists suggest that not all such hybrid viruses have pandemic potential.

RS and Parainfluenza Virus Vaccines

The respiratory syncytial (RS) and parainfluenza viruses are the principal causes of severe lower respiratory tract disease among infants and children. In fact, RS virus is probably the most important cause of death among the 10,000 to 12,000 infants who die each year from acute respiratory disease.

Bronchiolitis -- an inflammation of the lungs beginning in the smaller branches of the bronchial tree -- and pneumonia are the most serious manifestations of RS infection. The incidence of these two diseases when caused by the RS virus peaks at the age of two months. RS bronchiolitis falls off sharply after that age, and RS pneumonia decreases at a slower rate. NIAID grantees and contractors at the Washington, D.C., Children's Hospital found that 55 percent of infants under the age of six months admitted to their hospital for bronchiolitis had evidence of RS virus infection.

Obviously a vaccine for RS disease must be aimed at infants under two months old, but no vaccine has ever been evaluated in this young a target population. Infection with the RS virus begins in the upper respiratory tract, but in about half of very young infected children the virus spreads into the lower respiratory tract where it does most of its damage. This is where ts mutants could come into play. As in the case of influenza, a ts mutant virus vaccine administered intranasally should stimulate local antibody in the nose but not spread to the lungs.

Several years ago Dr. Chanock developed a promising ts mutant of the RS virus -- ts 1 -- which was manufactured and safety-tested by Flow Laboratories, under contract to NIAID. This vaccine was later tested at several institutions in infants over one year of age who already had antibody to RS virus. NIAID contractor

Dr. David Karzon is continuing to evaluate this live vaccine at Vanderbilt University. Further information is needed on the role of maternal antibody in the disease process and on the amount of virus excreted in various disease states.

Other clinical evaluations of the RS vaccine have been discontinued, however, because the occurrence of revertants (mutant viruses which have reverted back to the unmodified or "wild type") implies that this is still not the ultimate vaccine strain. Dr. Chanock and Dr. Robert Simpson, an NIAID contractor at Rutgers University, are both investigating other mutant vaccines, possibly involving a double mutation to attenuate the virus and significantly reduce the chances of reversion.

Drs. Chanock and Simpson are also looking for mutants of the parainfluenza viruses, for which no satisfactory live vaccine candidate has yet been found. Parainfluenza viruses are a common cause of pharyngitis, bronchitis, croup, and bronchopneumonia in children, and an occasional cause of upper respiratory tract infection and even pneumonia in adults. More than 32 percent of the croup patients at D. C. Children's Hospital were recently found to shed the paraflu virus in their respiratory secretions. Four types of paraflu viruses are probably responsible for as much as 20 percent of acute respiratory illnesses in children under the age of ten.

In a different approach, Flow Laboratories and Dr. John Gerin of the NIAID-AEC Molecular Anatomy (MAN) Program, funded in part by the Research Resources Branch of NIAID, are preparing inactivated and ultra pure parainfluenza virus types 1, 2, and 3 vaccines, as well as a trivalent (containing all three types) vaccine. The monovalent vaccines are now being studied in hamsters to determine their antigenicity and stability, along with the proper proportion of the three types for use in the trivalent vaccine. Once this preparation is ready, clinical trials using a vaccine prepared commercially under NIAID contract will be considered.

Adenovirus Vaccines

Of particular concern to the military is another acute respiratory disease caused by a group of viruses called the adenoviruses. Types 4 and 7 are most often involved in outbreaks of adenovirus respiratory disease in military training camps. Types 1, 2, and 5 are implicated in disease in children.

Vaccines against types 1, 2, 4, 5, 7, 14, and 21 have been tested in adults, and one for type 3 has been prepared, although clinical evaluation of it is not presently planned. Testing of vaccines for the pediatric types -- 1, 2, and 5 -- must await the determination of the appropriate pediatric formulation, as well as studies on subunit vaccines.

Subunit vaccines, similar in theory to the subunit influenza vaccines discussed earlier, are desirable since some strains and types of adenoviruses have been found to cause tumors in hamsters. The possibility of the strain in a live virus vaccine causing tumors in humans must be considered, although there are good reasons to believe this would not occur. A subunit vaccine would be free of material involved in tumor formation, the virus's genetic material, or nucleic acids. Dr. Julius Kasel, a former NIAID scientist, and another investigator in England, have prepared a crystalline adenovirus type 5 vaccine containing no nucleic acid. The vaccine has been shown to be antigenic and safe in adult volunteers at Baylor University and is now being tested in teenagers. Success in present evaluations will lead to trials in younger children.

Pneumococcal Vaccines

Bacterial diseases transmitted through the respiratory tract -- particularly pneumococcal pneumonia, meningococcal meningitis, *Haemophilus influenzae* type b infections, streptococcal infections, and tuberculosis -- also are of interest to the NIAID. Research supported or conducted by the Institute ranges from basic studies on the organisms to clinical evaluation of vaccines.

The pneumococcal organism, Diplococcus pneumoniae, occurs in more than 82 types, although only 14 of these types are implicated in the majority of pneumococcal infections. A normal inhabitant of the human upper respiratory tract, the pneumococcus may be harbored by 30 to 70 percent of all healthy persons at any one time. Illness occurs most frequently in individuals whose respiratory tracts have been weakened by viral infections, such as influenza, or by exposure to chemical or mechanical irritants. The chronically ill, as well as closed populations such as in schools or military installations, are also at risk.

Pneumococcal pneumonia is the most common form of this infection in the United States with at least 200,000 to 400,000 cases and perhaps 45,000 deaths attributable to this disease annually. The pneumococcus is also an important cause, especially in children, of otitis media (inflammation of the middle ear), meningitis (inflammation of the brain and spinal cord envelopes), and sinus infections.

The availability of sulfonamides, first used in 1938, and penicillin, introduced in 1943, provided new hope for those with pneumococcal infections. However, in recent years, the mortality rate for bacterial pneumonias is again on the rise. This is partially due to the increasing number of high risk elderly persons in the population. Another factor is the resistance that some pneumococcal strains have developed to penicillin, the main drug used in treatment.

An effective pneumococcal vaccine is, therefore, needed. In 1967 NIAID's Infectious Disease Branch began a surveillance program to identify the bacterial types most prevalent in pneumococcal pneumonia and the population groups at highest risk from pneumococcal infections. Once the 14 types were identified, work on a "polyvalent" vaccine began. Fourteen monovalent pneumococcal polysaccharide vaccines and three candidate polyvalent vaccines have been produced by Eli Lilly and Company under NIAID contract. These have been clinically evaluated for safety and antigenicity.

Field trials of these vaccines are underway at several institutions. The principal contractor under the program is Dr. Robert Austrian of the University of Pennsylvania. His laboratory serves as a central facility for analyzing epidemiologic and serological test data. In addition, under a subcontract between Dr. Austrian and Dorothea Dix Hospital in Raleigh, North Carolina, a field trial of the Lilly dodecavalent (twelve types) pneumococcal vaccine was begun in January 1973. Another field trial is being initiated at Kaiser Permanente Medical Center of San Francisco where an epidemiologic study was recently completed. Information on the effectiveness of this vaccine should be available in about two years.

Another field trial was in progress before 1973. NIAID contractor Dr. Arthur Ammann at the University of California, San Francisco, tested the 14 monovalent vaccines and one hexavalent (6 types) in children. Now an octavalent (eight types) vaccine is under study. Knowledge of the antibody responses of children to these antigens will assist physicians and scientists in their planning to prevent the illness and permanent disability associated with pneumococcal otitis and meningitis.

Success in this trial has stimulated interest of several pharmaceutical companies in development of pneumococcal vaccines. The techniques they are using to formulate their own vaccines are those developed under contract by NIAID.

Meningitis Vaccines

Meningitis can be caused by many different organisms, but bacterial infections are among the most serious. Extensive neurological damage and even death can result from such an infection. The three principal microorganisms causing bacterial meningitis are Neisseria meningitidis, called the meningococcus, Haemophilus influenzae or H. flu, and the pneumococcus.

H. flu has six types, of which type b is the most important cause of H. flu meningitis in infants and children under the age of three. Mortality is high among victims, and some degree of brain damage is evident in at least 50 percent of those saved by antibiotics. It is estimated that about 3,600 children showed permanent neurological defects in 1971 as a result of this type of meningitis. H. flu can also cause pneumonia, epiglottitis (inflammation of the epiglottis), and otitis media. Systemic infections with this bacterium seem to have increased in recent decades.

Two groups of investigators working independently with H. influenzae type b provided the basis for a vaccine by extracting the polysaccharide capsule or outer shell of the organism and showing that it was related to the development of immunity to the bacterium. Drs. David Smith and Porter Anderson at Children's Medical Center in Boston are now providing vaccine under NIAID contract to other Institute contractors at the Universities of Southern California, Colorado, and Rochester. These scientists are studying safety of the vaccine and optimum dosage in infants, as is Dr. Smith. He himself has developed sensitive assay techniques for determining antibodies and his laboratory serves as a reference laboratory for the entire program. The other developer, a former NIAID grantee, Dr. John B. Robbins, subsequently joined the National Institute of Child Health and Human Development (NICHD) where he continues his work. NICHD, through a contract with the Charlotte, North Carolina, Memorial Hospital, is now conducting a large field trial of efficacy of Dr. Robbins' vaccine and one for meningococcal type C in infants and young children.

Infants under 12 months of age, especially those four months old, are the target group for immunization with this vaccine, which has proven to be safe and antigenic in two-year olds, but not antigenic in the younger group. NIAID contractors are considering other ways to structure the vaccine to increase its antigenicity.

The aim of the Infectious Disease Branch program is production of a trivalent vaccine containing H. flu type b and meningococcal groups A and C. The meningococcus occurs in three groups, A, B, and C, and vaccines for groups A and C are now available from the Army for clinical testing. Eventually, the pneumococcal vaccine might also be included in a combined vaccine. Although meningococcal meningitis is not a respiratory disease *per se*, it is commonly transmitted through the upper respiratory tract.

NIAID contractors at the University of Southern California, University of Connecticut, and University of Colorado are all testing the Army group A and C vaccines in infants and children to determine safety and appropriate dosage levels. Rockefeller University has a contract to perform serological testing, including measuring antibody levels to determine response to the vaccines.

NIAID grantees, meanwhile, are exploring different approaches. Led by Dr. L. Barth Reller, scientists at the University of Washington have found that, in some persons, infection with non-disease producing strains of the meningococcal organism stimulates the production of cross-reacting antibodies that can kill other strains known to cause disease. This raises the possibility of stimulating protective antibody production in high-risk groups (such as military personnel) by deliberately exposing individuals to non-disease-producing strains of meningococci.

Mycoplasma Vaccines

Mycoplasmas, the smallest of free-living organisms capable of reproducing themselves without assistance from other forms of life, differ from both bacteria and viruses. Although implicated in a variety of illnesses, Mycoplasma pneumoniae is most often associated with respiratory disease, usually occurring in outbreaks during late summer and early fall. Young adults age 15 to 30 years old are at the greatest risk of M. pneumoniae infection which, though rarely fatal, is the cause of significant illness and absenteeism.

An inactivated M. pneumoniae vaccine was developed under NIAID contract at

Ohio State and Cornell Universities and tested for antigenicity and safety at the University of Virginia, Baylor University, and NIAID's Laboratory of Infectious Diseases. The Baylor study showed that although the intramuscular injection of the vaccine caused an impressive antibody response in the blood, it did not result in significant protection against experimental exposure to M. pneumoniae. Other studies showed the intranasal route of vaccine administration stimulated local antibody production in the upper respiratory tract and, thus, may provide protection. A small field trial of the vaccine in military personnel is now being considered by NIAID's Infectious Disease Branch.

NIAID scientists are investigating another approach to an M. pneumoniae vaccine. Drs. Robert Chanock and Harry Greenberg have developed and performed limited clinical trials of a ts mutant vaccine which appears to be genetically stable and to lead to antibody production. Dr. Chanock and his co-workers are also carrying out a variety of other experiments. He and Dr. Helmut Brunner, a visiting scientist from the Institute for Medical Microbiology in West Germany, have developed a sensitive new test for detection of antibody to M. pneumoniae. The test is a modification of a procedure known as radioimmunoprecipitation.

At the same time, Dr. George Kenny, an Institute grantee at the University of Washington, is studying both the chemical composition of the organism and reactions to the organism in human serum.

Streptococcus Vaccines

Group A streptococci, transmitted through the respiratory tract, cause a variety of diseases, but most commonly streptococcal sore throat (strep throat) and scarlet fever -- at least 421,517 cases in 1972. Acute glomerulonephritis (a serious kidney disease) and rheumatic heart disease of children are life-threatening aftereffects of streptococcal infections. Under an NIAID contract, Dr. Eugene Fox at the University of Chicago has developed and is now clinically evaluating M-protein vaccines for three types of streptococci.

Other investigations are focusing on more efficient methods for purifying M-protein of the streptococcus. In June 1973 a contract was awarded to Abbott Laboratories in North Chicago, Illinois, to produce crude streptococcal M-protein. When a sufficient quantity has been produced, it will be distributed to other researchers for purification. The final products will be compared for antigenicity.

Dr. Fox is also conducting basic studies of the chemical composition of the M proteins of Group A streptococci. To date he has found pronounced differences in antigenic composition between the strep involved in kidney disease and those isolated from the upper respiratory tract.

Tuberculosis Vaccination

A century ago, tuberculosis was so rampant in the United States that it was the leading cause of death. Improvements in living conditions and the introduction of effective drug therapy have led to a dramatic and steady decline in tuberculosis deaths over the past 35 years. Because of this progress, many people in the United States mistakenly believe that TB is no longer an urgent health problem. They are not aware, perhaps, that in 1972, 32,932 new cases of active TB were reported and that 5,567 people died from this disease as recently as 1969.

In the United States, prevention has focused on identifying infected individuals -- especially those who run the highest risk of developing active disease -- and treating them with drugs, primarily isoniazid, which is taken daily for one year. This procedure is preferred in the United States as a means of preventing tuberculosis, but a live vaccine, BCG, is widely used in many parts of the world.

BCG vaccination is effective only in those who have never had a primary infection. Drug prophylaxis, on the other hand, is intended for those who have already been infected, like most individuals in the United States who develop TB. For this reason, a mass program of BCG vaccination in this country has not been recommended by the Public Health Service.

One of the goals of researchers is to develop a more efficient tuberculosis vaccine or a better way of administering BCG. Scientists supported by a contract from NIAID's U.S.-Japan Cooperative Medical Science Program and others working in NIAID's Rocky Mountain Laboratory have recently found evidence that aerosol vaccination against tuberculosis is more effective than intradermal administration, the method most widely used today. Using rhesus monkeys which develop tuberculosis closely resembling the human disease, this team of researchers compared BCG vaccination by aerosol, intravenous, and intradermal routes. When they challenged the animals with small doses of virulent tuberculosis bacteria, they found that those monkeys vaccinated by the aerosol and intravenous routes had fewer signs of disease than the third group. These findings need to be confirmed in humans, but aerosol vaccination would lend itself readily to mass vaccination programs.

At the Rocky Mountain Laboratory, scientists have also been trying to develop an effective nonliving antituberculosis vaccine from purified fractions of mycobacteria. Many chemical, physical, and immunological techniques are being used to prepare and characterize the mycobacterial fractions from cell walls, cell membranes, and other components of several mycobacterial species and strains and to study the nature of the body's response to these fractions.

These studies also are expected to lead to an understanding of the role that BCG plays in cancer immunotherapy. BCG is being increasingly utilized in treating human cancer, but the basic action by which it retards tumor growth is poorly understood.

Fungal Infections

Respiratory disease -- both in the acute and chronic forms -- is also caused by a number of fungi or molds. The symptoms associated with these infections may vary from a mild, flu-like illness, to a serious and perhaps fatal systemic infection. NIAID is conducting research on various fungal organisms in its laboratories in Bethesda and supporting other studies through grants. Some of these infections are endemic in various areas of the United States -- such as histoplasmosis in parts of the eastern and central sections and coccidioidomycosis in the Southwest. Others may be devastating in certain groups of people; patients receiving immunosuppressive therapy for cancer or after an organ transplant are particularly vulnerable.

Outlook

Besides the National Institutes of Health, other government agencies are interested in many aspects of the problem of acute respiratory disease. The Center for Disease Control (CDC) maintains a surveillance of disease outbreaks and is responsible for identifying new influenza virus strains as they appear in this country. CDC also conducts tests of new vaccines and publishes, on behalf of the Public Health Service, recommendations for the use of approved vaccine preparations.

The Food and Drug Administration's Bureau of Biologics is responsible for setting standards for new vaccines and for ensuring that federally licensed manufacturers maintain these standards.

The Department of Defense's interest in acute respiratory disease stems from the major role these infections play in military recruit disability. Epidemiologic studies are conducted in military facilities throughout the world and some vaccine evaluation is performed.

The Department of Agriculture's support of work on influenza in animals is of interest to other scientists primarily because of the possible relationship between animal and human influenza.

Through the collaborative effort of these agencies and departments, vaccine development and testing are continuing. Information is exchanged among investigators, many of whom participate in NIH-sponsored workshops and conferences, designed to speed communication between scientists and develop an overall strategy against respiratory disease. When testing is completed the new vaccines will better control respiratory diseases, such as influenza and pneumonia, which endanger the health and curtail the productivity of millions of Americans. Other vaccines are expected to save thousands, especially children, from serious complications, including neurological damage, which may follow certain bacterial infections.

CLINICAL VIROLOGY

Mr. **Flood**. Take a look at page 279 of your justifications. There you state:

> . . . the Institute is initiating a program of clinical virology.

Suppose you tell the committee about that new effort and how you think that will contribute to reducing the influenza problem.

Dr. **Davis**. This program, which is under development at the present time, is intended to increase the capability of scientists located in hospitals and laboratories in the detection and diagnosis of influenza and other virus diseases.

There is a considerable gap in the general practice of medicine in specifically diagnosing virus diseases. The techniques are difficult and very expensive. It is not nearly the simple thing that it is in bacterial diseases or parasitic diseases.

Our effort will be directed toward improving techniques for diagnosis and providing training for people in the area.

Mr. **Flood**. For the record, what is the difference between a virus and a bacterium?

Dr. **Davis**. A virus is a very small organism which lives in cells. A bacterium is a larger organism which sometimes invades cells but often lives in between cells. It can grow on artificial media. Viruses require living cells for their growth.

Mr. **Flood**. Do they reproduce sexually?

Dr. **Davis**. Viruses are reproduced by damaging the cell itself. With their enzymes they take some of the protein of the cell and recombine it into their own structure.

The bacteria grow in the tissues in between the cells. There is no evidence that viruses have any sexual cycle at all.

Mr. **Flood**. Do either of these affect the reproduction of the cell itself?

Dr. **Davis**. Yes. The viruses actually in most cases destroy the cells.

Mr. **Flood**. It will prevent reproduction of a cell itself?

Dr. **Davis**. Yes, it prevents the reproduction. It destroys the cell in most cases. In some cases it persists within the cell and its genomes can be incorporated into the cell and may carry on for many generations.

PNEUMONIA VACCINE

Mr. **Flood**. With reference to pneumonia, in your budget justification you say:

> A vaccine for the prevention of bacterial pneumonia has been developed and currently is being field tested. It is expected that within the next 2 years there will be a product ready for licensure.

I hope you are right. That is good news for a change.

When this vaccine is marketed, will it be one of those wonder drugs with a high price tag on it, and that's it?

Dr. **Davis**. We think not. The vaccine, of course, is made from bacteria. It is always much cheaper to make vaccines from bacteria than viruses.

The other thing is that it is made from the polysaccharide coat of the bacteria. It is a very potent vaccine, and a little bit of it goes a long way. We anticipate it will be a relatively inexpensive vaccine.

Mr. **Flood**. Thank goodness.

How frequently will someone, say an elderly person, receive such a vaccine in order to be protected against bacterial pneumonia?

Dr. **Davis**. This is one of the good things about this vaccine. The evidence now is that the immunity produced by these bacterial pneumococcal antigens lasts for a long time, 5 years or longer. So, it is quite a different story from the influenza story, where we have to be vaccinated every year.

VACCINES TO BE FIELD TESTED

Mr. **Flood**. You also state in your justifications that you are developing other vaccines which are about to be field tested.

Tell us something about some of these other vaccines, especially when you think you will have a safe product that you can market.

Dr. **Davis**. The other vaccines to which we are referring are against bacterial meningitis. This disease is primarily of infants and children. It is caused by two principal types of bacterias, meningococcus and the second principal type is the hemophilus influenzae type b. These, like the pneumococcus, have a capsule or coating on the bacteria which is polysaccharide in nature, and also produces a very good antigen.

Techniques have been developed within the last 4 or 5 years for extracting and purifying this and a vaccine. It is now being tested in several places in the country—Connecticut, Los Angeles, and Colorado—against meningitis in children.

Mr. **Flood**. What about cholera?

Dr. **Davis**. The vaccine against cholera has been developed through a great deal of work. This is a little different type of vaccine. It is what we call a toxoid because the cholera organism does its damage by producing a toxin or poison, so the vaccine is developed against that.

This has been developed. It has been manufactured. We have a supply of it on hand. We are making arrangements now to field test it in Bangladesh.

As you know, the mouth of the Ganges River is the center of cholera. Cholera occurs there all the time.

STREPTOCOCCAL DISEASE

Mr. **Flood**. The second part of my question was: When do you think you will have a safe product on the market for these vaccines against the two we are talking about now, meningitis and cholera? You did not mention anything about streptococcal disease. What about that?

Dr. **Davis**. Streptococcal disease is a very difficult one. We do have studies going on for a vaccine against that. That is another type of vaccine. We have one grant and one small contract for vaccine against streptococcal disease. It is very difficult.

Mr. **Flood**. When do you think you will have a safe product on the market?

Dr. **Davis**. There would not be any product on the market unless it was safe. I am sure we all agree to that.

If the tests turn out well for pneumococcus, we expect that will be in about 2 years.

The meningococcus may be a little longer, because it may take longer to demonstrate its effectiveness.

Mr. **Flood**. Is there any way we can accelerate this process? Is there any way you can speed up the tests so we can have a safe product on the market as soon as possible?

Dr. **Davis**. Yes. We can have more studies going on than at the present time.

Mr. **Flood**. This is a bad thing for me to ask you, but will more money shorten the process?

Dr. **Davis**. In this instance, yes.

V.D. DIAGNOSTIC TEST

Mr. **Flood**. How about venereal disease? Last year you told us, and I am going to quote:

> Just recently a blood test has been devised which will improve our capability of decreasing gonorrhea very markedly. The investigator thinks he will probably have this blood test ready within a year, and a commercial house is interested in producing it.

Where do you stand on this test? Is it ready to be marketed?

Dr. **Davis**. This is still under investigation. We understand the commercial house is still interested in it. They are developing it.

The basic principle of the test is holding up, which is essentially that this is a development of a diagnostic antigen prepared from the pili on the coat of the gonococcus which is very specific.

Mr. **Flood**. You told us what it is. I am concerned now about the readiness. You said it would be ready in a year. It was a big deal last year. And here we are. We always come back. Here it is. Is there anything on the market?

Dr. **Davis**. It is not ready now.

Mr. **Flood**. All right. How close is it? What are you going to say this year?

Dr. Davis. I would be afraid to say almost anything this year. We are working on it.

Mr. **Flood**. There is not much sense now in asking you this. How expensive will it be to administer, if and when?

Dr. **Davis**. The first estimate was that it would be relatively inexpensive.

Mr. **Flood**. That is what you said, yes. You still hold to that?

Dr. **Davis**. Yes.

Mr. **Flood**. We are spending $24.8 million at the Center for Disease Control, the CDC, to operate a national venereal disease control program. Are there any other inexpensive tests anywhere on the horizon at all that will help these CDC people in this control program; some kind of test that would be simple and inexpensive for this kind of thing?

Dr. **Davis**. I think the tests that I have just been speaking to should be helpful to them and to everyone else who is concerned about this.

GONORRHEA

Mr. **Flood**. We do not seem to be getting anyplace with you fellows about this business of why the repetition of infection without developing any resistance. One dose, six doses, seven doses.

What about this kind of thing? You can cure them all except the first one, that kind of talk. Where are we on that? We do not seem to be able to develop any immunity. There are repeated infections in one person.

Dr. Davis. This is one of the puzzling things about gonococcal infections. It could be due to one of several things. One is that there are different strains, and there is evidence that there are different strains of the gonococcus which have different antigenic characteristics, something like the influenza virus, where you might be protected against one but not against others.

There is also reason to think that there may be other growth differences of the different strains of gonococcus so the individuals respond differently.

These are some of the fundamental things that we do not really understand.

Mr. Flood. I went through this last year and the year before. Why is it that one person can have a series of infections? You are indicating why. It is due to different types of strains. Even that is vague.

Is it your shop or in whose shop would there be a revival of or the beginning—there never was one very much compared to cancer and other things—of a public relations operation to spread knowledge and information in all areas, regardless of age, on the dangers of these gonorrheal infections?

There is no spreading of information. There is no intelligence, no warning, no danger signs or anything. Who should be doing that?

Dr. Davis. No, Mr. Chairman, we have not been involved in demonstration or public education. This has traditionally for many years been the responsibility of the Center for Disease Control. As you know, they have a Division of Venereal Disease down there. It was only 2 or 3 years ago that we realized our fundamental knowledge of the diseases, and particularly the organisms which caused them, was indeed very bad.

As I mentioned earlier, from practically a zero base a few years ago, we are now planning to spend $2.6 million in 1975.

Mr. Flood. What happens? What may be the result of gonorrhea and what may be the result of syphilis to the person, to the victim? You say that is not handled by you. I am talking to the wrong people, then.

Dr. Davis. We do not have the facilities for disseminating the information.

TUSKEGEE STUDY

Mr. Natcher. Dr. Davis, what part has your Institute played in the Tuskegee case, the matter pertaining to syphilis, which has been going on for a number of years? Are you in that as far as the Institute is concerned?

Dr. Davis. The NIAID and NIH have never had any involvement in the Tuskegee case.

BONE MARROW TRANSPLANTS

Mr. Flood. On immunology research, last year we were very excited. You began to talk to us about bone marrow transplants. That was something. Transplant bone marrow? We thought that was something. We thought bone marrow was something nobody dared even touch.

What we were talking about was very primitive, of course, because of the immunological problems involved, naturally.

You seem to have come a long way since last year. I have an article here from the Washington Post of March 26, headed, "Marrow: Leukemia Nemesis."

I am sure you have seen this article, which talks about a successful bone marrow transplant. Is this procedure at the point now where people with leukemia can look forward to a cure?

Dr. Davis. I think we can be very hopeful about that. The number of bone marrow transplants is increasing each year.

In 1973, for instance, Mr. Chairman, our record shows there were 96 bone marrow transplants in the United States, most of these at the University of Washington where there is a very large center. Half of these were for leukemia.

At the present time, about one-third of those patients are still alive.

The other principal reason for bone marrow transplants is aplastic anemia. It is a very promising thing.

Actually, the records show that there have been a total of 181 bone marrow transplants in the last 3 or 4 years.

EDUCATING PHYSICIANS

Mr. Flood. How do you go about training or familiarizing more physicians with this procedure so more people can avail themselves of this? Maybe doctors are so busy they do not read the newspapers. How are we to get to the physicians to train and familiarize them with these procedures so people know about them?

Dr. Stone. Might I respond to that, Mr. Flood?

We have been talking about a possible role for NIH in direct education of physicians in regard to such very new procedures.

Mr. Flood. I talked to a doctor on the phone just this week who himself has leukemia, and he had never heard about this.

Dr. Stone. We think we might have a role in doing that kind of education.

Existing on the NIH campus is a Foundation for Advanced Education in the Sciences that was organized by members of the NIH staff. Dr. Stetten is a past president of it. We think there might be a role for the foundation, together with the NIH, in providing just that kind of educational opportunity for physicians who might come and live in Bethesda for a week or a few days at some kind of conference center. We would like to do that.

Mr. Flood. I am telling a doctor who has leukemia about this great idea. This fellow is no amateur. He is quite a guy.

Dr. Stone. Some of this, when it gets in the newspaper, is still quite experimental. Sometimes the press is talking with more enthusiasm than knowledge.

IMMUNOLOGY RESEARCH

Mr. Flood. Are there any other exciting projects now underway in the area of immunology research that you would like to tell us about?

Dr. Davis. I would like to speak for a minute again about asthma and allergies.

I mentioned there is a new drug now on the market in this country, sodium cromoglycate, which is extremely effective in the treatment of allergy, particularly in children. It is very useful because you do not need to use as many of the steroid or cortisone drugs.

This has a different kind of action from the kind of drugs used formerly. It attacks the problem right in the cell where the mediators are being formed and released. It is a very promising drug.

One of the most interesting advances is in the sensitivity to bee sting. As you know, probably 100 people die every year with anaphalactic shock from bee sting. This has been a very difficult problem to handle.

Now scientists in two places, Baltimore and Buffalo, supported by our allergic disease centers, have developed mans of purifying the venom from individual kinds of wasps and bees so they can make a specific diagnosis.

Mr. FLOOD. For the record, let us have a half dozen of those besides the bee sting, something more widely spread and more concerning the general public, so we have a half dozen of these new immunology research programs.

[The information follows:]

EXAMPLES OF RESEARCH PAYOFFS IN THE AREA OF IMMUNOLOGY

TRANSPLANTS

Increased understanding of the role various organs and blood components play in the immune response has led to the development of ways the system can be reconstituted. For example, transplants of thymus tissue or bone marrow are being used to correct certain congenital defects or treat a disease process.

DIAGNOSTIC TESTS

The radioimmunoassay, which measures very small amounts of clinically important substances in the blood, has been adapted for use in screening blood donors in order to prevent transmission of the agent causing serum hepatitis.

HEREDITARY ANGIOEDEMA

Hereditary angioedema—HANE—is an illness in which frequent attacks of swelling, or "giant hives", throughout the body result in death in about 25 percent of cases. Recognition of HANE as an immunologic disorder has led to the development of drugs which, essentially, cure the disease.

TRANSFER FACTOR

Soluble material—transfer factor—obtained from the white blood cells of specifically sensitized donors, is being used, experimentally, to treat immunologically deficient patients with diseases such as leprosy, candidiasis, and Wiscott-Aldrich syndrome. Transfer factor has also been found useful in helping certain cancer patients fight off recurrences of their malignancies.

PREVENTION OF RH DISEASE

A striking success in regulation of the immune response has been use of anti-Rh antibodies to prevent an Rh-negative mother carrying a Rh-positive child from producing more antibodies which will harm the child. Wide use of this approach has virtually eliminated this once all-too-common and often fatal disease—erythroblastososis fetalis.

HEPATITIS

Mr. FLOOD. On hepatitis, in your general statement you certainly seem to have made considerable progress in that disease. You say as a result of your efforts to distinguish between hepatitis A and hepatitis

B you might develop a simpler test for diagnosing the infectious form of the disease. How do you use that word "simpler"? I hope it means inexpensive.

Dr. DAVIS. The test would be simple if you have an electron microscope.

Mr. FLOOD. Do you mean inexpensive too? Do they go together?

Dr. DAVIS. Yes, this should be a simple and relatively inexpensive test if the equipment is already there.

Mr. FLOOD. I am thinking about the man in the street with these things. What about the inexpensive thing?

Dr. DAVIS. Of course this is very early, Mr. Chairman, in the development of this technique, so that we don't know how much it will finally be refined. The principle is very simple. It is just observing whether or not these viruses are clumped by serum from the patients who may or may not have the infection.

Mr. FLOOD. What is the change? As a result of what your people are doing are you reducing say, by 50 percent, the number of deaths resulting from hepatitis B?

Dr. DAVIS. Serum hepatitis. The hepatitis B of course is a different disease really from hepatitis A.

Mr. FLOOD. I mean the serum hepatitis.

Dr. STONE. The national blood program addresses itself to that—particularly in an effort to have hospitals utilize only volunteer donors. We are taking two parallel courses. One is the development of some kind of a vaccine which would prevent infection and, on the other hand, to control the supply of infected blood.

DIAGNOSTIC TESTS FOR HEPATITIS

Mr. FLOOD. Will you be able to test the donor before he gives the blood to determine if he has hepatitis? It has everybody scared to death.

Dr. DAVIS. Yes. These tests are already being used.

Mr. FLOOD. That question is red hot.

Dr. DAVIS. There are really two kinds of tests that can be used to test the blood of a potential donor to see whether or not he has the antigen. There is also another test which detects whether or not he has the antibodies which might indicate that some time in the past he has had the disease but may no longer have it. I think most blood banks now, submit the donor's blood to the test to see whether or not it has hepatitis B antigen known as the Australia antigen. This test, the radioimmunoassay test, is much more sensitive than the previous tests.

We think soon we will be able to show a diminished incidence and in fact we already have shown it. I don't have the figures for that but my impression is that the incidence of transfusion hepatitis is diminishing.

Mr. FLOOD. I would like you to develop the answer to that on the record when you get it because that is right out in front right now, the business of testing the donor on hepatitis.

[The information follows:]

Preliminary data from the national hepatitis surveillance program show a decline in the total number of reported viral hepatitis cases associated with transfusion for 1972 and 1973 when compared with previous years; however, the

Center for Disease Control stresses that this surveillance program depends on voluntary reporting by individual doctors and detects only a fraction of the total number of cases that occur. In addition, transfusion-linked cases have represented a continually decreasing percent of total reported hepatitis B cases, declining from 55.2 percent in 1966 to 13.6 percent in 1972.

At the NIH Clinical Center there has been a 75 percent reduction in post-transfusion hepatitis as a combined effect of both the elimination of commercial blood and the testing of all donors for the hepatitis antigen.

Mr. PATTEN. We are hearing from the surgeons because in the case where they want to use blood, people are refusing to take it when they are being operated on—unrelated to your hepatitis—because of the publicity. I have had surgeons tell me that they are being hampered in their work on account of what the chairman is stating.

Dr. DAVIS. I think this is very justifiable.

Mr. FLOOD. Mr. Michel.

Mr. MICHEL. Thank you, Mr. Chairman.

Doctor, the chairman has pretty well covered this in his items. I would like to turn to the justification figures themselves.

IMPOUNDED 1973 FUNDS

You have an unobligated balance restored of $10,408,000 of funds previously impounded and then released. Is that right?

Dr. DAVIS. Yes.

Mr. MICHEL. What effect does the release of that $10.5 million have in your shop?

Dr. DAVIS. It permitted us to pay some research grants that were approved in 1973, but for which we didn't have funds.

Mr. MICHEL. Because they were approved did they automatically get awarded, or since another year's time has lapsed was there another look to see if they were as good a year later as when you were about to approve them?

Dr. DAVIS. They compare very well from 1 year to another. But the grant applications which were awarded from 1973 funds were very high quality. They were certainly in the upper half of those which were deemed meritorious by the Study Sections.

Mr. MICHEL. Is that really where most of the money has gone, into the awarding of grants?

Dr. DAVIS. Yes, into the awarding of grants.

The largest amount as shown on page 266 went into paying some of the training grants which were approved in 1973 and fellowships also. And some in research and development contracts.

The difference between the figure you see there and the $10 million is money which went to support the general research support grants administered by another division of NIH.

Mr. MICHEL. I understand from the committee staff that you are probably going to submit a new table or series of new tables.

Dr. DAVIS. Yes.

EXPLANATION OF BUDGET TABLES

Mr. MICHEL. Notwithstanding that, let me ask you, on page 256, will those new tables clear up the distorted picture I get here as I read through that justification? I see "research grants, noncompeting continuations regular program", an increase of 12, another increase of 12, and then we go down to decreases. We have minus 11, minus 16, minus 39 and a lot of minuses. It looks about like the same type, the research grants noncompeting, up and down, and it looks like fellowships are up and down and training grants up and down. I feel like I am on a yoyo. How do you account for this?

Dr. DAVIS. I will ask Mr. Magruder to answer that.

Mr. MAGRUDER. This is a mechanism we use to show where our programs increase and decrease in a year, and I think these new tables will help satisfy you.

Mr. MICHEL. It is confusing when you read this. It is going around the mulberry pole. I suspect if I added and subtracted the figures, eventually they come out to what these totals represent. What I am interested in is when we go on the floor members want to know are we doing more or less overall in this Institute, are more people being trained or less, are there more grants being awarded or less?

Strictly on balance in answer to those who might say "I see this net change of minus $6.6 million" I think our answer to that obviously is that those figures are no more meaningful today in view of the release of funds which added the additional amounts to be spent in fiscal 1974. Is that right?

Dr. DAVIS. I agree.

Mr. MICHEL. That is all, Mr. Chairman.

Mr. FLOOD. Mr. Smith.

OVER-THE-COUNTER DRUGS

Mr. SMITH. There are several patent medicines for allergies, some of which apparently work pretty well for some people. Yet I hear that the way they make them effective is that they put in whatever is needed to take care of all kinds of allergies so they will be bound to hit the one someone happens to have. Is this a correct statement?

Dr. DAVIS. In general it is, because the drugs and the inhalants which are used for asthma and for hay fever attack the result of the immunologic process.

When a person is exposed to a pollen or something which causes asthma, the cells produce chemicals which we call the mediators. These are histamine and slow reacting substances, et cetera.

The logic of the treatment is to neutralize those substances, and this is what the antihistamines do. Histamine, for instance, is the substance which causes a runny nose, eye swelling, and the chemicals that are in the drug neutralize those substances.

Dr. STONE. The FDA, as I believe you might know, is engaged in a very extensive review of all over-the-counter medication which falls into this category. They have convened panels of individuals to review such drugs and to decide which of them are effective and which are ineffective and to take off the market those in which there are multiple components, some of which are expensive but not useful for the allergy in question.

Mr. SMITH. My question goes to those that are effective. What are the other side effects?

Dr. STONE. That, too, is primarily an FDA problem. That is, from the perspective of NIH, it is something which falls within the purview of FDA.

Mr. SMITH. What if someone secures some medication for something else and they also have been accustomed to taking one of these patent medicines for their allergies, and they continue to take that, too?

DRUG SURVEILLANCE PROGRAM

Dr. STONE. We do have in Boston, and I might ask Dr. Stetten to comment, the drug surveillance program.

Dr. STETTEN. There is an extensive program in Boston, run by a Dr. Hershel Jick who is associate professor of medicine at Boston University School of Medicine, which is an intensive screening procedure of predominantly in-hospital patients in which complete records are kept of the medication which they have been taking, the assortment of signs and symptoms they exhibit, and the final diagnosis—all under hospital scrutiny.

This study has turned up a number of unexpected so-called adverse drug reactions, which have become apparent because a large sample of the population is being studied. A sample on the order of 25,000 patients is under scrutiny.

Mr. SMITH. How is this study being financed?

Dr. STETTEN. This is being financed by contracts from the National Institute of General Medical Sciences. At this time, a coordinating committee, with representation from the Food and Drug Administration and several of the Institutes of Health, is studying the problem of how this may be more effectively financed on a continuing basis.

Mr. SMITH. Is enough being done to determine the adverse effects of mixing these kinds of drugs and warning people they should not do so? That is really my question.

Dr. STETTON. I would say a reasonable effort is being made in this direction. Enough is never done.

Mr. SMITH. I ask that question in light of the fact there are so many millions of people that take these antihistamines. It seems anymore almost everyone is subject to some allergy, and they find out one of those patent drugs takes care of it. I don't think they are being warned when they are given a prescription for something else that you shouldn't take an antihistamine while taking this.

Dr. STONE. You are right on target. No question. It needs our collective attention.

Dr. DAVIS. There are an enormous number of these drugs being used as you mention. Our figures show there is $254 million every year spent for drugs for asthma and hay fever.

Mr. SMITH. Is that up substantially?

Dr. DAVIS. It is increasing every year. I don't have the figures for previous years but this is for one of the last several years.

Mr. FLOOD. Mr. Patten.

Mr. PATTEN. Doctor, my advice to you is to buy stock in my pharmaceuticals because the pill business is getting better.

Dr. DAVIS. I can't do that, sir. I have the wrong job.

Mr. PATTEN. You can form a trust or something.

When I was mayor we had 800 cases of venereal disease, and we started a clinic at the local hospital. Dr. Cottrell wrote me a 10-page letter against clinics.

You say you are just starting on VD in the last few years and putting up a few dollars. Of course at the State level we have had the Wasserman for certainly over 30 years, and I know the Army has a few dollars in their budget on this subject. And there is activity all over the world with our military insofar as the VD problem is concerned.

Is there coordination of effort here of the municipal effort? Locally, in the District of Columbia. I read in the paper there is an epidemic. You hear so often the amount of VD is of epidemic proportions. Yet you speak of adding another million.

Do you think the amount of money you are using under your new program is adequate considering the size of the problem?

Dr. DAVIS. No, there are always many opportunities to do things. As I said, we have increased our investment over the last few years.

Mr. MICHEL. With the prodding of this committee.

Dr. DAVIS. Yes. Together with the Center for Disease Control, we have submitted a special report on venereal disease to the committee.

Mr. PATTEN. How about the Surgeon General and the doctors in the military and Navy and all as well as our health departments at the State level and universities? Are they doing research?

Dr. DAVIS. They are not doing quite the same kind of research. They are investigating problems for instance of efficacy of treatment, what kinds of treatment are the best, how do people react to different treatments. This is also being done by the Communicable Disease Center which has the major role for the Public Health Service in VD.

Mr. MILLER. There is $28 million in the budget for CDC for venereal disease.

Mr. PATTEN. It just struck me, considering the enormity of the problem we hear every time we turn around in our cities, after all the years and the money being spent at the local and State levels I wonder if we are getting the best out of the dollars we spend, like the $28 million you have now?

Would you say at all levels of government there is a better approach?

Dr. DAVIS. We are trying to find a better approach, but it is clear that the methods which have been used in the past 20 or 30 years are not solving the problem. Our intent when we embarked on this was to try to develop some new information, some new knowledge which might lead to better ways of preventing it.

For instance, we traditionally always think of a vaccine against venereal disease. The fact was we didn't know enough about the organisms to try to devise a vaccine. For instance we can't grow the spirochete in artificial media. We don't have any ways of getting large amounts of it the way we can other microbial agents. We didn't know until a few years ago what the structure of the gonococcus was, what its antigens were that might be effective. We have to know more about the fundamentals of organisms that cause it.

Mr. FLOOD. You didn't know the structure of the Gonococcus?

Dr. DAVIS. We knew what it looked like, but we didn't know what kind of membranes or protein it had. Now we know there are two layers to the membrane which surrounds the organism. And through some studies in New York Rockefeller University scientists detected in one of those layers several proteins, one of which is antigenic.

These are the kinds of things we know about other organisms, but because very little research was done on these diseases for the past 20 or 30 years since penicillin came in we thought we had the problem licked. Now we have to go back and start again and get some new approaches. That is what we are trying to do.

Mr. MICHEL. Isn't it true generally, Doctor, that this has been our problem? The State and local communities have contented themselves with their expenditure for simply treatment and care, but there weren't the resources for getting a new avenue of research to combat it. We satisfied ourselves with a good shot of penicillin and we contented ourselves with that for a number of years. It is only in the last few years we are getting down to the nitty gritty of trying to find a new research answer to it. I think that points up again the justification for research at a national level. We have a problem of trying to get that kind of money together in the State and local communities. It is just impossible.

Dr. DAVIS. That is right. I might point out we expect to fund about 25 grants this year, and in addition we have three large program project grants which will look at the problems comprehensively, under review. How those will fare I don't know, but there is a great escalation of effort directed toward this.

ASTHMA AND ALLERGIC DISEASE CENTERS

Mr. PATTEN. Doctor, you said you have established 17 centers in 13 States for a program of asthma and allergic diseases and you support it with $1.6 million. Can we have a list of where those facilities are for the record?

Dr. DAVIS. Yes. I have it here.

Mr. PATTEN. Is there one in the Metropolitan New York area? We get a lot of inquiries and don't know what to tell people.

Dr. DAVIS. At the present time there is not one in New York. The nearest I suppose would be Baltimore and Boston. They are scattered about the rest of the country. San Francisco, St. Louis, California.

[The information follows:]

ASTHMA AND ALLERGIC DISEASE CENTERS

Robert Bent Brigham Hospital, Boston.
Washington University Medical School, St. Louis.
Johns Hopkins University School of Medicine, Baltimore.
Children's Asthma Research Institution and Hospital, Denver.
University of Wisconsin School of Medicine, Madison.
Scripps Clinic and Research Foundation, LaJolla.
National Jewish Hospital and Research Center, Denver.
University of California at San Francisco, San Francisco.
Northwestern University Medical School, Chicago.
Louisiana State University School of Medicine, New Orleans.
University of Michigan Medical Center, Ann Arbor.
Mayo Graduate School of Medicine—New York, Rochester.
State University of New York Buffalo General Hospital, Buffalo.
Medical Center, NIH, Bethesda.
Duke University School of Medicine, Durham.
University of Colorado School of Medicine, Denver.
Creighton University School of Medicine, Omaha.

Mr. **Patten**. That is all.

Mr. **Flood**. Mr. Obey.

Mr. **Obey**. Thank you, Mr. Chairman. I have just a couple of questions.

FELLOWSHIPS AND TRAINING GRANTS

First of all I am not the old hand on this committee like everybody else is. Can you explain for my benefit what is the difference between the recipient of the scholarship and the recipient of the training grant?

Dr. **Davis**. A fellowship is awarded to an individual on his own application.

Mr. **Obey**. I understand that.

Dr. **Davis**. A training grant is given to a department in a university which then makes its own selection of their trainees.

Mr. **Obey**. I understand that. What I am trying to get at, is there any difference in the kind of individual who is likely to get one versus another?

Dr. **Davis**. I don't know there is really very much. A fellow can choose wherever he wants to go, and anywhere.

Mr. **Obey**. Is one any further along?

Dr. **Davis**. Up until recently the training grants were awarded for some who had not yet received their Ph. D., their doctor's degree. This was true also I believe for fellowships up until recently. So I think they both cover that. There are special fellowships which were awarded to scientists who were pretty well along in their career and wanted to make a change, move into a new area or learn some new techniques or get some new concepts they didn't have before.

Dr. **Stone**. There is this operational distinction: The trainees under a training grant, being selected by the institution, might be somewhat younger individuals because they are known to be preceptors in the institution, whereas individuals who are competing for fellowships on a national basis, where the selection is central, might, perhaps, be a little further along in their development. But those are tendencies rather than clear differences.

Dr. **Stetten**. There is the additional difference that, in the awarding of a training grant, it is the institution and the department and the responsible trainer who are under scrutiny by the review committee. Therefore, presumably, there has been a careful and precise selection of the best centers for training. The fellow, having acquired his fellowship directly, is essentially free to select any site for his training.

Mr. **Obey**. I understand the difference and I understand the argument about whether you are going to be helping strengthen the individual institutions or not.

Dr. **Stone**. I would think a mix of the two is what we ought to strive for.

NEW TRAINING PROGRAM

Mr. **Obey**. Secretary Weinberger said in his statement:

> In the area of biomedical research rather than general across-the-board training we have instituted a new program of postdoctoral fellowships in priority biomedical research areas.

I would like your personal and professional opinion on this. First of all, do you think the thrust of the administration's policy change is helpful in your area?

Dr. DAVIS. Yes and no. I think it does help us to focus a little better on areas where we need more trained individuals. For instance, the area of venereal disease, one of our difficulties is we don't have enough people trained in research, and this program would permit us to do that in a good way.

Clinical allergy is another such area. But it does not provide the same kind of overall experience in research training that we formerly had.

TERMINATION OF TRAINING SUPPORT

Mr. OBEY. And that is how it is not helpful in your judgment.

Last year in the discussion I had with you, you said:

> The ability of microorganisms to develop resistance to antibiotics is responsible for continuing additions to the list of infectious diseases which no longer will respond to such treatment.

You mentioned gonorrhea and a number of others.

This morning I received some letters from Dr. Michael Rotel who is head of the Department or Infectious Diseases at what was formerly known as Marquette Medical School.

One paragraph says:

> I would like to briefly illustrate just one problem area that may be of interest to you and certainly of great importance to the health of the people in Wisconsin. This has to do with the termination of support of the training grants for young doctors that want to go into specialty training. I would like to use for an example my own subspecialty. That is infectious diseases. At the present time there is only a handful of trained infectious disease specialists in the State of Wisconsin. The members of our subspecialty are called upon to advise doctors on diagnosis and treatment of infectious diseases including selection of antibiotics. As you know, antibiotics are the most frequently prescribed drugs in this country. Unfortunately it is quite apparent they are frequently overprescribed and at times inappropriately selected and administered. This has resulted not only in additional expense to the public but has also led to disastrous clinical results in many cases. Because it appears it would be very difficult to train additional specialists in this field under the present NIH funding program, I am sure the situation regarding antibotics used in Wisconsin will not improve in the foreseeable future.

What I would like from you is an answer to this question: Is he wrong and, if he is, why?

Dr. DAVIS. I think he is very correct. We see this everywhere. Throughout the country there seems to be a lack of people who are trained and expert in managing these infections which are still occurring, particularly in hospitals now.

Mr. OBEY. You say he is correct in his assumption that termination of support of training grants will hamper any change in that?

Dr. DAVIS. I was answering the first question. He is right in that this is a very serious problem.

Mr. OBEY. What about his assertion that termination of support of training grants will create great problems in achieving any improvement in that area?

Dr. DAVIS. I would have to say personally I would agree.

Mr. OBEY. Thank you.

FEDERAL ROLE IN TRAINING

Mr. MILLER. Could I add a little bit which I hope doesn't quarrel with the last exchange? But all of the conversation we have had during this hearing about training grants and fellowships seems to focus on, whether one of fellowships or training grants.

I don't think the Government policy has been to make a choice which says that a fellowship is good and a training grant is not the right way to go about acquiring trained researchers. I think the question has been for the past 2 years "What is the Federal role?" I don't think this has been discussed enough. Dr. Stone started to make this point several days ago but didn't develop it very much.

I think the administration is saying we were too abrupt in 1974, and we are willing to come back and take a look at where there might be a more legitimate Federal role than we saw previously, and we said that role should be to identify the specialty areas where the researchers are not being produced and where we can clearly not rely on the marketplace, and it is too urgent for us to wait to see if our policy of relying on the marketplace will develop those researchers.

We said that in the postdoctoral area these specialties can be developed better through fellowships. I think we are saying, however, with the marketplace and with the continued hopeful support of training grants from sources other than the Federal Government, we will still hope to have a sufficient number of trained researchers.

Mr. OBEY. Mr. Weinberger indicated that under this new program the postdoctoral fellowships in priority biomedical research areas they expected to support no more than 3,700 researchers in 1975 under that program. I would assume since there are many other areas competing for the term "priority biomedical research areas" we would not serve as many in your area. Is that true, Doctor?

Dr. DAVIS. Yes.

Mr. OBEY. Thank you.

CONTRACTS

Mr. CONTE. You have a big switch from research grants to contracts in the area of bacterial and fungal diseases. Are all of the new contracts in the VD program, or were more subareas affected?

Dr. DAVIS. The new contracts will not be limited to the VD program. There will be a significant increase in efforts to evaluate vaccines against pneumonia and bacterial meningitis and in contract activities related to the prevention of hospital-associated infections.

SPECIAL GRANTS VERSUS CONTRACTS

Mr. CONTE. What is a special grant and how it is distinguished from a contract?

Dr. DAVIS. A special grant as used in the budget narrative table, page 268, is a budget term for awards made for certain planned programs. Currently, special grants are used to support three types of activities—scientific evaluation, the research career development program, and centers for selected purposes. The awards are grants in aid made with the intention of providing maximum investigator flexibility but they are judged by the same dual review system as regular project grants.

The research contract on the other hand, is a conventional legal agreement to undertake certain research activities in pursuit of a defined objective. NIAID contracts are used exclusively to support developmental research designed to accomplish predetermined program objectives that are part of an established targeted or developmental program.

INVESTIGATOR MEETINGS

Mr. CONTE. The annual meeting of directors of your asthma research centers looks like a good way to coordinate a program like that. Do you have similar meetings with people holding research grants for work in the same area?

Dr. DAVIS. At present the only annual meeting held for investigators in a specific area of research is this one for directors of our Asthma and Allergic Disease Centers. We invite other investigators to meet, from time to time, in workshops called to discuss discrete research problems. For example, several very valuable workshops have been arranged for individuals working on various aspects of immunology research, hospital associated infections, or vaccine development.

TRANSFER FACTOR

Mr. CONTE. If further tests of the use of transfer factor in treatment prove successful, how great are the production problems?

Dr. DAVIS. We are told by experts in this field that the technology for producing transfer factor is known. Problems arise, however, in recruiting suitable donors and in obtaining their white cells which contain specific transfer factor. A feasibility grant at Stanford University supports the use of a cell separator unit which, at present, is supplying enough transfer factor for limited use in a few specific diseases. Large volumes of blood must be taken from which white cells can be separated and the other components returned to the donor. I would say that, at present, production problems are certainly significant.

ORGAN TRANSPLANTS

Mr. CONTE. How many organ transplants, of all kinds, are performed in this country annually?

Dr. DAVIS. According to preliminary data received by NIAID, transplant operations performed in this country in 1973 amounted to 3,139, including 3,000 kidneys; 20 hearts; 21 livers, 96 bone marrows; 1 pancreas; and 1 thymus. Figures are not available on skin or cornea transplants.

Mr. CONTE. What is the longest time before rejection?

Dr. DAVIS. The greatest risk of rejection occurs during the first 3 months posttransplantation. After 2 years, rejections rarely occur but patients have rejected their transplanted kidneys as long as 5 years postoperatively. Patients who have received kidney transplants should remain on immunosuppression for the rest of their lives but the dose of drugs is often markedly reduced after several years.

Mr. CONTE. You describe some theoretical ways of getting around transplant rejection—enhancement and tolerance. Are you beyond the theoretical stage yet—that is, are you doing any actual experiments with either technique yet?

Dr. Davis. In man, these procedures are still theoretical. Animal models are being developed, however, and in time these procedures may be ready for clinical application.

[The following additional material was furnished for the record:]

ORGAN TRANSPLANTATION

It has been almost 20 years since a vital organ -- a kidney -- was first transplanted successfully from one person to another, and, in that case, the donor and the recipient were identical twins. Only in the last 10 years has organ transplantation been achieved between persons not bound by the close biological ties of twinship.

Through 1972 -- according to the American College of Surgeons-NIH Organ Transplant Registry -- over 15,000 kidneys have been transplanted. Hearts (227), livers (200) and other organs, too, such as lungs (32), and the pancreas (32) have also been transplanted.

NIH-supported research has provided most of the knowledge which has made these transplant operations possible. Although problems are far from solved, a successful transplant operation is truly a "miracle of modern medicine." Thousands of men, women, and children are now enjoying a normal or near normal life, thanks to the gift of a functioning organ. Thousands of others still wait for that miracle. It has been estimated that at least 8,000 Americans each year would benefit from a kidney transplant. Figures are not available on potential recipients of other organs.

Obligations for programs in organ transplantation (in thousands)

	1971	1972	1973	1974 estimate	1975 estimate
National Institutes of Health:					
National Institute of Allergy and Infectious Diseases...	$4,254	$4,496	$3,457	$4,126	$3,680
National Institute of Arthritis, Metabolism, and Digestive Diseases..................	4,331	4,973	5,992	6,554	6,759
National Cancer Institute.....	880	1,809	1,539	2,113	2,285
National Heart and Lung Institute......................	2,335	2,408	2,972	3,100	3,300
Division of Research Resources.................	3,054	3,823	3,473	3,673	3,273
TOTAL..........	$14,854	$17,509	$17,433	$19,566	$19,297

NATIONAL INSTITUTES OF HEALTH

National Institute of Allergy and Infectious Diseases

NIAID Collaborative Program

Matching Donor and Recipient of Organ Transplants. In the fall of 1964, the National Institute of Allergy and Infectious Diseases (NIAID) established a collaborative program in immunology to provide information needed by investigators working in the field of organ transplantation. Scientists had just begun to use drugs to suppress the body's tendency to reject foreign tissue and the transplantation of organs had thus become a therapeutic possibility for persons with kidney and other serious diseases.

On the advice of a panel of experts, the Institute gave first priority in its transplantation program to the acquisition of sera (the clear portion of the blood) which would be useful in "matching" organ donors and prospective recipients. Research had established that substances present on an individual's lymphocytes (white blood cells) determine the so-called "compatibility" of his tissues with those of another person. These inherited substances, known as histocompatibility (HL-A) antigens are grouped in two close-linked series. This means that each person has no more than four such antigens -- two handed down from his father and two from his mother.

The blood of some individuals -- women who have had several pregnancies, or persons who have received multiple blood transfusions -- contains specific antibodies (protective substances) to HL-A antigens. Sera from these "immunized" persons can be used as typing reagents to identify the HL-A antigens on any individual's white cells.

If a patient needs a transplant, a member of his immediate family usually makes the best donor since there is a one in four chance of brothers and sisters having inherited identical antigens from their parents. Typing sera is used to pick the best "match" among family members. It has now been established that transplants between siblings with the same HL-A antigens do better than transplants between siblings who are identical for only one-half of the HL-A antigens. These, in turn, do better than transplants between siblings who have no HL-A antigens in common.

Evaluating Matching in Unrelated Donors and Recipients. Unfortunately, the large number of possible HL-A combinations makes it quite difficult to match all four antigens of unrelated donors (usually cadavers) and recipients and only slightly less difficult to match for two or three. In a recent NIAID computer analysis of typing data on nearly 2000 kidney transplants, poor matches predominated for cadaver transplants. In spite of the fact that more than 65% of all kidney transplants now utilize an unrelated donor, conclusive information is not currently available to determine the utility of matching in such procedures.

The National Institute of Allergy and Infectious Diseases, on the recommendation of its Transplantation and Immunology Advisory Committee, has now embarked on a carefully planned effort designed to study the efficacy of tissue matching in cadaver kidney transplants. Data will be collected and analyzed on approximately 3000 kidney transplants during the three-year-period starting January 1974.

Contracts have been awarded by NIAID to six regional groups participating in this study. The contractors for this study are: the Cleveland Clinic, Cleveland, Ohio; the University of Utah Medical Center; the University of Illinois College of Medicine; the University of Rochester; the University of Texas Medical School; and the University of Minnesota Medical School. The investigators will use standardized NIH materials and methods to type donors and recipients. Clinical data will be reported on standardized forms developed by a statistical center which will also analyze the information collected.

A statistical services contract has been awarded to the University of North Carolina. In addition, a group of eminent immunologists, kidney specialists, surgeons, and statisticians are serving as a panel of experts to share with NIAID staff the responsibility of planning and supervising the evaluation.

Tissue Typing and Reagents. Closely related to the evaluation study is the Institute's continuing support, through contracts, of the development and use of effective tissue typing materials and techniques. When the collaborative program started, only two HL-A antigens were recognized in man. Now, at least 32 antigens have been recognized and there is good indication that others may be involved in HL-A compatibility.

Unfortunately, sera which identify only one antigen are still not available in sufficient quantities to permit accurate typings. Most sera contain antibodies to multiple antigens and computer analyses are often necessary to define individual antigens adequately. Good sera for the important but infrequently found antigens are still virtually nonexistent and apparent cross-reactions make it difficult to recognize some antigens in the presence of others.

As a research service, NIAID provides typing sera of the highest quality obtainable through its serum bank and NIH typing tray program. The serum bank now stores approximately 1300 different reagents. Additions to the bank are obtained by contract, by donations from serum users, or by direct purchase.

The NIH Tray. In 1971 NIAID established a standardized typing tray. This has permitted typing for known HL-A antigens with a constant set of high-quality reagents. A new tray, developed during 1973, contains 70 of these reagents which identify 32 antigens. The tiny wells of this small plastic tray are preloaded with minute amounts of sera prior to distribution to typing laboratories. When a transplant operation is contemplated, scientists test white blood cells of the organ donor and of prospective recipients against sera in the trays. That individual whose array of HL-A antigens most closely matches those of the organ donor is chosen as the actual recipient. During 1973 more than 1800 trays were distributed to 125 laboratories.

The quality of these sera and their effectiveness in tissue typing is regularly monitored by independent laboratories and by NIAID staff receiving reports from tray users. Annual workshops are sponsored to promote the exchange of knowledge on tissue typing techniques and a tissue typing manual and a catalogue of reagents are prepared periodically by NIAID staff.

A serious problem in organ transplantation is the frequent existence in a recipient's blood of what are known as "preformed antibodies." These substances are thought to result, primarily, from sensitization to cells of multiple blood transfusions, such as kidney patients often receive. Identification of these antibodies would provide an additional means for excluding unsuitable donors.

Work is now underway to produce a NIH multiwell tray loaded with viable human cells which can be used as a uniform source of histocompatibility antigens. Testing against these cells should help determine the presence and identity of preformed antibodies in a patient and should alert the physician to those donor HL-A antigens which will precipitate almost immediate rejection of a donated organ.

Recent technical developments which permit bulk sera to be freeze-dried for shipment to investigators have resulted in remarkable savings for the reagents program. When bulk sera had to be shipped by air in specially constructed insulated containers with large quantities of dry ice, an average U.S. shipment cost $25.03. Now sera can be sent in smaller, non-refrigerated packages by ordinary mail at an average cost of $1.97.

Immunosuppression Studies. Even when organ donor and recipient are well-matched according to typing data, some degree of suppression of the immune response must usually be employed to protect the transplant from rejection. In general, this is accomplished through the use of drugs, such as Azathiaprine and/or a biological preparation known as anti-lymphocyte serum (ALS).

ALS is an immunosuppressive agent prepared by injecting lymphocytes of one species into animals of another. For example, mouse ALS can be prepared by injecting mouse lymphocytes into guinea pigs and then withdrawing from the guinea pigs sera containing specific antibodies to the mouse lymphocytes.

For a number of years, NIAID operated a sub-human primate testing facility for ALS. Investigations in over 250 animals at this facility revealed that human thymus cell antisera prepared in rabbits consistently prolonged skin grafts in monkeys and chimpanzees. A sufficient amount of this material has now been prepared under an exchange of funds agreement with the National Medical Research Institute (NMRI) to make possible a carefully designed study of the effectiveness of this preparation in transplant patients.

Approximately 60 percent of U.S. transplant programs use various ALS preparations as adjuncts to immunosuppressive drugs, but no well-conducted clinical trials have been carried out.

The University of California at San Francisco has agreed to conduct clinical trials of the rabbit ALS in collaboration with NIAID and the Navy. The study will involve 50 patients and 50 controls and is expected to take two years. Two additional years will be required for follow-up.

In the meantime, the primate testing facility has been closed out. The Navy, however, will continue studies in monkeys, baboons, and chimpanzees of any toxicity leads which may result from the clinical study.

Plans are underway to launch new studies of procedures to modify immune responsiveness. These may include a number of "immunological tricks." Some of these have been tried in animals but have not been adequately studied in patients. The new program on manipulation of the immune response will seek to develop and investigate methods for "turning up" or "turning down" the body's natural defenses against disease agents and foreign tissue.

Research Accomplishments of NIAID Program. As NIAID's collaborative program in transplantation immunology begins its 10th year, a review of research accomplishments attributable to program activities seems appropriate. For example, the first contract awarded -- one to investigators at the University of California, Los Angeles -- resulted in the development of a laboratory technique which is now the standard procedure in tissue typing. This same contract supported the development of the NIH typing tray, a multiple serum syringe, and a transport system which permits mailing blood samples for typing. Computer programs for analysis of typing data were also developed.

A contract awarded in 1966 to a Canadian worker led to his discovery of the mixed lymphocyte culture (MLC) reaction which was then used by NIAID grantees in further research which resulted in a second test for histocompatibility.

Using procedures developed by NIH intramural and grant scientists, an industrial laboratory, funded by an NIAID contract, developed large-scale processes for the production of functionally active components of human complement -- an important participant in the immune response. This laboratory is now marketing the first commercially produced human complement.

There is much more evidence of the productivity of NIAID's collaborative organ transplantation effort. Drug protocols, laboratory equipment, and serological techniques have all come out of this program. In each instance, as soon as the feasibility of a new product or technique was established, the private sector was encouraged to take over and governmental support was terminated. This partnership effort has, thus, spearheaded many of the exciting advances being made in one of the most dramatic and fast-moving areas of medical research.

Grant-supported Work

Many National Institutes of Health grants are awarded to teams of non-Federal investigators who are engaged in research on different facets of organ transplantation. A few examples of this grant-supported research follow.

Heart Transplants. At Stanford University, California, Dr. Norman E. Shumway's group, supported by grants from the National Heart and Lung Institute and from the Division of Research Resources, reported recently that between January 1968 and January 1973, they performed heart transplants in 52 patients. During this period, 85 patients had been admitted to hospital as potential recipients. At the time of reporting 4 still awaited transplants but 29 had died before a suitable donor became available. The fact that the mean survival time of these patients after selection was only 21 days dramatizes the severity of disease present in all potential heart transplant recipients.

During this five-year period at Stanford, results have improved significantly with the one-year survival of patients receiving transplants during 1971 reaching 50%. For the whole series, one-year survival is 41% and two-year survival is 37%.

The investigators found that the principal determinant of long-term survival is the successful management of acute rejection episodes during the first two months after the operation is performed. Early detection of rejection, through careful monitoring of the patient, including electrocardiograms twice daily, and use of a new technique whereby actual samples of the transplanted heart tissue are obtained and examined microscopically for signs of rejection permit early treatment with the required immunosuppressive drugs.

Bone Marrow Transplants. The National Cancer Institute (NCI) is conducting research on bone marrow transplantation as a possible treatment for patients who have lost the ability to produce normal blood cells. Bone marrow transplantation might benefit some patients with leukemia, a form of cancer in which defective white blood cells replace normal blood cells and are often produced in abnormally large numbers. This procedure might also be useful in treating patients with aplastic anemia, a non-cancerous disease in which red and white blood cells and platelets are produced at low levels or not at all, as well as individuals whose marrow had been destroyed by anticancer drugs or radiotherapy.

Because the bone marrow and its cellular products are immunologically active, donated bone marrow can afflict the recipient with a serious condition called graft-versus-host (GVH) disease. This is a critical problem even when donors are close relatives. Research on GVH disease includes studies of bone marrow antigens and of ways to limit the marrow's immune activity, particularly by using an antiserum directed against the marrow's white blood cells. This latter approach is under evaluation at the National Cancer Institute in Bethesda and at the University of Washington, Seattle. Other studies at NCI are aimed at exploring removal of some marrow from a patient made free of cancer symptoms, for return to the patient later if the cancer recurs. Much of this research is being done in experimental animals, as well as in patients where all other treatments have failed.

Since 1969, Dr. E. Donnall Thomas and co-workers at the University of Washington School of Medicine, supported by both the National Cancer Institute and the National Institute of Allergy and Infectious Diseases, have performed bone marrow transplants. In the first 49 patients with far advanced acute leukemia not responding to drug treatment, and in 24 patients with aplastic anemia, the scientists found that the transplants permitted treatment with otherwise lethal drugs and radiation, resulting in disappearance of symptoms of the disease in about one-fourth of the acute leukemia patients for periods from 8 months to 3-1/2 years. About one-half of the aplastic anemia patients had normal marrow function restored for 8 months to 2-1/2 years. Graft-versus-host reactions occurred in about 70 percent of patients in the two groups. In about one-fourth, severe reactions hastened death.

Kidney Transplants. Dr. Joseph J. Kaufman, a grantee of the National Institute of Arthritis, Metabolism, and Digestive Diseases (NIAMDD) at the University of California, Los Angeles, has been engaged in research on renal arterial hypertension -- a kidney disease which in some patients with severe high blood pressure, particularly those in the younger age group, can be rapidly fatal. For the past 10 years or so, surgeons have been treating this condition by repairing the affected kidney artery. Dr. Kaufman has developed a new surgical procedure which involves moving the kidney itself into a position in the body where it can be attached to a healthy artery.

Dr. Kaufman performed his first "autotransplant" five years ago in a seven-year-old boy who was near death. Today the patient is living a normal life. In all, Dr. Kaufman has performed seven such operations in which the kidney is moved within the patient's body. Recently, Dr. Kaufman removed a kidney and kept it viable in a new solution while he and other surgeons carried out various necessary surgical procedures in the patient.

Dr. Kaufman sees many uses for autotransplants, especially in conjunction with the new solution which was developed at UCLA. He suggests, for example, that a kidney full of stones could be removed, put in solution, and "workbench surgery" performed on it before putting it back in the body.

For years the value of kidney transplants for children was questioned since it was believed impossible to regulate the amount of immunosuppression needed so that normal growth could take place. Now, however, it has been shown that children actually need less in the way of suppression than adults and that they are among the best candidates for transplantation.

At Children's Hospital Medical Center in Boston, grantees of NIAMDD and DRR have reported a 95% one-year survival rate for kidney transplants in young patients. Dr. Raphael Levey, associate professor of surgery at Harvard and director of Children's Hospital dialysis unit, points out that, in addition to needing less suppression, children are free of the degenerative diseases such as heart attacks, which plague older patients.

The latest report of the Kidney Transplant Registry -- a part of the ACS/NIH Registry -- indicates that mortality following transplantation in large medical centers (more than 25 transplants annually) was only half that in smaller centers. There is reason to believe that this discrepancy may be even greater than the data indicate. According to a recent survey, only 70% of the U. S. transplants are being reported. The nonreporting centers are all small and their results may be even poorer than those of the centers which do report.

This finding that hospital size plays a role in the successful transplantation of kidneys may have special meaning in view of recent changes in Medicare which now covers all costs of transplantation and/or dialysis.

VACCINE TESTING

Mr. Conte. Your plan to seek college students, instead of prisoners, as subjects for testing candidate vaccines raises some serious problems. Students are under serious economic pressures and there is a real question if this makes their participation truly voluntary. Have you subjected this plan to scrutiny by any advisory group that includes members from outside the scientific community?

Dr. Davis. Yes. Needs for such volunteer facilities for phases I and II testing of candidate vaccines against respiratory diseases have been discussed with the NIAID Infectious Diseases Advisory Committee and with other Government agencies. Any such facility must have the approval of its parent university administration and research review committees as well as established NIH review groups. Further, individual projects will have to receive advance review in both university and NIH channels. All work is open and available to public review at any time. Protection against financial or other inducements which may influence volunteers is a matter of specific inquiry in all such research.

ETHICAL REVIEWS

Mr. Conte. In this regard, do your intramural scientists and contractors have to submit their research to the same kind of ethical review as research grantees?

Dr. Davis. Yes. Projects proposed by intramural scientists in clinical research have been subject to external review processes by bodies including nonscientist membership for the past 20 years. Contracts involving human subjects receive, in addition to the usual primary and secondary reviews, a separate review by a NIH-constituted review board of the clinical protocol in regard to need for the work, risk benefit evaluation, validity of the protocol to provide important data, adequacy of informed consent procedures, and ethical considerations. Proof of approval by the institutional committee of the proposed contractor is a prerequisite to NIH approval.

BLOOD DONORS

Mr. Robinson. With respect to serum hepatitis, what is your current view of the problem as related to blood collection by blood banks—nonprofit and profit?

Dr. Davis. The sooner we go to an all voluntary donor system the sooner we will reduce serum hepatitis. There's no doubt about it. By employing an all-voluntary donor system and by screening and eliminating hepatitis B positive blood, the Nation's blood banks should be able to cut transfusion hepatitis by more than half. More research will be needed to get a further reduction.

Mr. Robinson. Is there a continuing problem in regard to the collection of blood from derelicts for pay?

Dr. Davis. The problem is probably being reduced. Once we go to the voluntary system of blood donors, the problem should be diminished. It is reasonable to assume that derelicts would not give blood to the extent they sell it today if the monetary incentives are eliminated.

VENEREAL DISEASE

Mr. Robinson. In the matter of venereal disease screening, what is your estimate of undetected cases? I have in mind the incidence among young people of infections not identified until they have progressed to a serious stage.

Dr. Davis. The Department estimates that there are approximately 2.5 million cases of gonorrhea occurring each year in the Nation. The vast majority of these cases occur in persons from 12 to 29 years of age. Of this number between 600,000 and 800,000 are asymptomatic and therefore have greater potential for progressing to serious stages of the disease. The exact number who progress to late complications is unknown, but generally believed to be about 20 percent. During the period July 1972 through February 1974, 9,944,000 women were screened for gonorrhea; 466,000 were infected and approximately 95 percent of them received treatment, thus preventing them from progressing to a serious stage of the disease.

RESEARCH DISSEMINATION

Mr. Robinson. You have mentioned a number of encouraging developments in the area of your research concerns. What does your Institute do to disseminate the information to the medical profession? I have in mind the general practitioner in the small community in my congressional district. I should like to think that the results of tax-supported research would be made directly available to him by some means other than the visit of the drug company salesman.

Dr. Davis. Of course, our scientists and grantees are encouraged to publish their results in medical journals and to present their findings at scientific and medical meetings. These results are often published in specialty publications as well as in the Journal of the American Medical Association, the New England Journal of Medicine and several others that are directed toward physicians in general practice. We also are in continual contact with representatives of the medical press, who distribute controlled circulation publications to the medical professions.

Science writers, particularly those based in the Washington area, attend our briefings on discoveries in allergic and infectious disease research. For example, during the last annual meeting of the American Academy of Allergy we had 10 physicians and scientists at the meeting in Florida on a 2-way telephone hook-up with science writers located in our Institute conference room in Bethesda. These investigators were discussing their presentations so the science writers could inform their readers, including physicians, of the latest advance.

Our Institute has recently developed a series of publications on allergic diseases for the lay public, and individual copies have been sent to allergists throughout the country indicating their availability to patients through the Government Printing Office. Each of the leaflets includes a section on research. We feel that "the word gets out" on most important research accomplishments but we are planning to increase our efforts to "educate" the physician on the application of research results to patient care.

HEPATITIS

Mr. Robinson. You mention encouraging progress in terms of finding the causes of viral hepatitis, the first step toward prevention of this disease. How would you visualize that the progress so far made would be transmitted into techniques that would prevent the spread of hepatitis which we know has been caused by blood transfusions from hepatitis affected victims?

Dr. Davis. We believe that, at present, a combination of limiting donations to volunteers rather than commercially purchased and screening by laboratory tests for presence of the hepatitis B antigen could reduce the incidence of transfusion hepatitis by more than half.

INFLUENZA

Mr. Robinson. If the influenza virus which is being tested in Texas is found to be safe and successful, how long would it be before it would be available for general use?

Dr. Davis. Following testing of the neuraminidase-specific vaccine in Texas, our Institute is planning to initiate a field trial of the vaccine in children in Buffalo, N.Y. If the vaccine continues to prove safe and protective, it should be available to manufacturers for production in approximately 2 years. If it does not afford a high enough level of protection, we will continue our efforts to find other improved methods of protection against influenza.

CHOLERA

Mr. Robinson. Have there been identified instances of Asiatic cholera in the United States? If so, how many?

Dr. Davis. There was one case last year, in Texas. This was the first since 1911.

PENICILLIN FAILURES

Mr. Robinson. You mention the problem caused by patients who are truly penicillin-treatment failures with respect to venereal disease treatment. What portion of patients so treated fall in this category?

Dr. Davis. According to information from the Center for Disease Control, 5 to 6 percent of gonorrhea patients are truly penicillin failures and 8 to 9 percent of gonorrhea patients are truly ampicillin failures.

HAY FEVER AND ASTHMA

Mr. Robinson. Ragweed is mentioned specifically with regard to therapy for hay fever. Is ragweed still considered to be the most difficult and prevalent of plants causing hay fever?

Dr. Davis. Ragweed is considered the most common cause of hay fever in North America. It has been estimated that one plant, during the "hay fever season," produces as many as 1 million grains of pollen per day.

Mr. Robinson. Regarding the new asthma drug, disodium cromoglycate, is this felt to be a broad-base drug to prevent asthmatic attacks or is it felt that it will be mainly useful for some sort of specific asthmatic conditions in patients? What is the incidence of growth being affected by children who have used steroids for a prolonged period of time?

Dr. Davis. Studies have shown that disodium cromoglycate is effective to some degree in about 50 percent of adult asthmatics and in as many as 85 percent of pediatric patients. It is a preventive, not a treatment, however, and its use does not abolish the need to determine the cause of the patient's asthma and to provide relief of symptoms. The drug is most helpful as a prophylactic for the patient with predictable seasonal attacks of some severity. However, each patient must be individually studied.

Theoretically, the bone growth of all children treated with steroids is affected. The effect, however, in any patient is somewhat related to his age and is definitely related to the dosage and duration of treatment. Growth of youngsters in late adolescence is not as adversely affected as is that of younger children. In many patients, alternate day steroid therapy has been found successful both in regard to management of their disease and diminution of side effects of the drug.

Mr. Flood. Thank you, gentlemen.

JUSTIFICATION OF THE BUDGET ESTIMATES

NATIONAL INSTITUTES OF HEALTH

National Institute of Allergy and Infectious Diseases

Amounts Available for Obligation[1/]

	1974 Revised	1975
Appropriation	$114,000,000	$110,404,000
Amount withheld (PL 93-192)	-3,596,000	
Subtotal, adjusted appropriation	110,404,000	110,404,000
Real transfer to:		
"Departmental management" (For Department-wide reductions in public affairs)	-35,000	---
Comparative transfers to:		
"Office of the Assistant Secretary for Health" (Transfer of administrative support activities to the Office of the Assistant Secretary for Health)	-60,000	---
"Departmental management" (Transfer of accounting functions from the OS Working Capital Fund)	-8,000	---
Comparative transfers from:		
"Departmental management" (Transfer of indirect cost negotiation function to the OS Working Capital Fund)	10,000	---
"National Institute of General Medical Sciences" (Decentralization of scientific evaluation grants program)	150,000	---
Subtotal, budget authority (base obligations)	110,461,000	110,404,000
Unobligated balance, restored	10,408,000	
Comparative transfer of restored unobligated balance to Research Resources for General Research Support Grants	-3,819,000	
Total, obligations	117,050,000	110,404,000

[1/] Excludes the following amounts for reimbursable activities carried out by this account: 1974 - $460,000; 1975 - $400,000.

Summary of Changes

1974 Estimated obligations	$117,050,000
1975 Estimated obligations	110,404,000
Net change	-6,646,000

	1974		Change from 1974	
	Pos.	Amount	Pos.	Amount
Increases:				
A. Built-in:				
1. Annualization of pay raise	---	---	---	+$141,000
2. Within grade increases	---	---	---	+300,000
3. Wage board pay raise	---	---	---	+40,000
4. FTS rate increases	---	---	---	+50,000
5. BEC rate increase	---	---	---	+5,000
6. Extra day of pay	---	---	---	+46,000
7. Increased cost of service and supply	---	---	---	+130,000
8. Payment to NIH management fund	---	---	---	+350,000
Subtotal				+1,062,000
B. Program:				
1. Research grants				
a. Noncompeting continuations regular program	---	---	---	+12,270,000
b. Competing grants - regular program	---	---	---	+12,372,000
c. Special program	---	$4,584,000	---	+310,000
2. Fellowships				
a. Noncompeting continuations	---	---	---	+1,899,000
b. Competing	---		---	+2,760,000
3. Training Grants - Noncompeting continuations	---	---	---	+4,301,000
4. Research and development contracts	---	11,842,000	---	+2,630,000
5. Intramural laboratory and clinical research	479	13,700,000	---	+167,000
Subtotal				+36,709,000
Total, increases				+37,771,000
Decreases:				
A. Built-in:				
Annualization of average grade reduction in 1973	---	---	---	-88,000
B. Program:				
1. Research grants				
a. Noncompeting regular research grants completed or converted to competing status	---	43,166,000	---	-11,118,000
b. Competing regular research grants completed or converted to noncompeting status	---	16,364,000	---	-16,364,000
c. 1974 obligations used to fund 1975 continuations	---	3,934,000	---	-3,934,000

2. Fellowships				
a. Noncompeting fellowships completed or converted to competing status.....	---	95,000	---	-95,000
b. Competing fellowships completed or converted to noncompeting status..	---	3,129,000	---	-3,129,000
c. 1974 obligations used to fund 1975 continustions.	---	428,000	---	-428,000
3. Training grants				
a. Noncompeting training grants completed or converted to competing status................	---	6,425,000	---	-6,425,000
b. 1974 obligations used to fund 1974 continuations.	---	700,000	---	-700,000
4. Research and development contracts				
a. Research and development contracts completed.....	---	11,842,000	---	-2,136,000
Subtotal................				-44,329,000
Total, decreases.........				-44,417,000
Total, net change......................				-6,646,000

Explanation of Changes

Increases:

A. Built-in:

These increases will provide $141,000 for annualization of Federal Pay Comparability Act pay raises enacted in calendar year 1973; $300,000 for within grade pay increases; $40,000 for wage board pay increases; $50,000 for increased costs in 1975 for use of the Federal Telecommunications System (FTS); $5,000 for increased Bureau of Employee Compensation (BEC) rates; $46,000 for one extra day of pay in 1975; $130,000 for increased costs of service and supply, and $350,000 for increased costs for centrally furnished services.

B. Program:

1. Research grants
   a. The amount of $12,270,000 in noncompeting research grants represents increased costs of previously awarded grants plus 185 "new" continuations resulting from grants made in 1974 Although the total number of noncompeting continuations decreased by 84 between 1974 and 1975, the average grant size increased by approximately $7,000 and hence the total cost increased by $1,152,000.

b. The amount of $12,372,000 in competing research grants reflects: (1) $6,830,000 for approximately 108 new awards; (2) $5,262,000 for 84 competing continuations; and (3) $280,000 in supplementals.
c. The increase of $310,000 for special program will provide funding for an additional 12 research career awards for a total of 93 awards in 1975.

2. Fellowships
   a. The amount of $1,899,000 in noncompeting fellowships represents the "new" continuations resulting from awards made in 1974. The number of continuations increased by 110: from 12 in 1974 to 122 in 1975.
   b. The amount of $2,760,000 in competing fellowships provides funding for 137 new awards.

3. Training grants - The amount of $4,301,000 will provide funding for 56 noncompeting continuations.

4. Research and development contracts - The amount of $2,630,000 will provide funding for increased cost of contracts plus approximately 12 new contracts and 12 contracts converted to non-competing.

5. Intramural laboratory and clinical research - The amount of $167,000 will provide for increased research emphasis on better diagnosis and correction of immune disorders and on virus diseases.

Decreases:

A. Built-in:

The decrease of $88,000 is for annualization of savings for the average grade reduction in 1973.

B. Program

1. Research grants
   a. The amount of $11,118,000 represents approximately 269 noncompeting regular research grants that were completed in 1974 or that are being converted to competing status in 1975.
   b. The amount of $16,364,000 reflects the completion or conversion of 220 competing grants to a noncompeting status.
   c. The amount of $3,934,000 reflects the reduced funding required in 1975 due to the multi-year funding of 83 projects in 1974.

2. Fellowships
   a. The amount of $95,000 represents 12 noncompeting fellowships that were completed in 1974.
   b. The amount of $3,129,000 reflects the completion or conversion of 181 competing awards to a noncompeting status.
   c. The amount of $428,000 reflects the reduced funding required in 1975 due to the multi-year funding of 29 projects in 1974.

3. Training grants
   a. The amount of $6,425,000 represents 64 competing training grants that were completed in 1974.
   b. The amount of $700,000 relects the reduced funding required in 1975 due to multi-year fund of 15 projects in 1974.

4. Research and development contracts
   a. The amount of $2,136,000 represents the completion of 12 contracts in 1974 and 12 contracts that were converted to a continuing status.

Obligations by Activity

Page		1974 Base*		1975 Estimate		Increase or Decrease	
Ref.		Pos.	Amount	Pos.	Amount	Pos.	Amount
269	Allergic and immunologic diseases......	---	$27,758,000 (29,505,000)	---	$27,218,000	---	-$540,000[A/] (-2,287,000)
274	Bacterial and fungal diseases...........	---	23,941,000 (27,020,000)	---	23,992,000	---	+51,000[B/] (-3,028,000)
278	Viral diseases........	---	21,801,000 (23,344,000)	---	21,888,000	---	+87,000[C/] (-1,456,000)
283	Parasitic diseases....	---	10,578,000 (10,798,000)	---	9,782,000	---	-796,000[D/] (-1,016,000)
286	Intramural laboratory and clinical research...........	479	20,479,000	479	21,562,000	---	+1,083,000[E/]
291	Research management and program services	117	5,904,000	117	5,962,000	---	+58,000[F/]
	Total obligations (bases).	596	110,461,000	596	110,404,000		-57,000
	Total obligations.........		(117,050,000)				

Explanation of Changes

A. The decrease of $540,000 reflects somewhat less support for the overall spectrum of research programs represented by this activity. However, research in the Special Emphasis Program areas will be high-lighted. The Institute objective to reduce morbidity due to asthma and allergic disease will be managed through regular research projects and the coordinated efforts of the Asthma and Allergic Disease Centers. Plans are being made to expand clinical immunology and immunopathology research so as to benefit the patient whose immune system is depressed either through deficiencies of his own system or secondary to other diseases or drugs. Transplantation research will be modestly expanded. Studies to improve in quantity and quality the reagents available to perform typing for transplantation and transfusion will continue.

B. The increase of $51,000 reflects somewhat greater support for the overall spectrum of research programs represented by this activity. Increased emphasis will be given to research on infections complicating hospitalization. A research program for the ultimate control of venereal disease through improved detection and immunization methods will be emphasized. Also, it is planned to field test vaccines for bacterial pneumonia, meningitis and cholera.

C. The increase of $87,000 reflects somewhat greater support for the overall spectrum of research programs represented by this activity. Research on influenza and other respiratory diseases will be emphasized. The development and evaluation of a vaccine against hepatitis B will be a major objective as well as the identification and characterization of the agent of hepatitis A.

D. The decrease of $796,000 reflects less support for the development of fundamental information required to achieve the long-range goals of effective prevention and control of parasitic diseases and control of disease vectors. However, new initiatives will be undertaken in such areas as further research on the unusual form of hydatid disease and the mechanisms of immunity against disease organisms in vectors.

E. The increase of $1,083,000 reflects a net mandatory increase of $916,000 and a program increase of $167,000 for increased research on better diagnosis and correction of immune disorders and on virus diseases.

F. The increase of $58,000 reflects a net mandatory increase related to personnel costs.

*Excludes 1973 appropriation restorations.

Obligations by Object

	1974 Estimate	1975 Estimate	Increase or Decrease
Total number of permanent positions	596	596	---
Full-time equivalent of other positions	50	50	---
Average number of all employees	665	649	-16
Personnel compensation:			
Permanent positions	$9,543,000	$9,982,000	+439,000
Positions other than permanent	315,000	315,000	---
Other personnel compensation	425,000	425,000	---
Total personnel compensation	10,283,000	10,722,000	+439,000
Personnel Benefits	1,407,000	1,413,000	+6,000
Travel and transportation of persons	425,000	450,000	+25,000
Transportation of things	95,000	95,000	---
Rent, communications and utilities	450,000	500,000	+50,000
Printing and reproduction	105,000	105,000	---
Other services	2,133,000	2,082,000	-51,000
Project contracts	11,842,000	12,336,000	+494,000
NIH Management fund	8,105,000	8,455,000	+350,000
Supplies and materials	2,700,000	2,972,000	+272,000
Equipment	680,000	730,000	+50,000
Grants, subsidies, and contributions	78,825,000	70,544,000	-8,281,000
Total obligations by object	117,050,000	110,404,000	-6,646,000
Total obligations excluding 1973 appropriation	110,461,000		

Significant Items in House and Senate Appropriations Committee Reports

Item	Action taken or to be taken
1974 House Report	
1. The Committee expects that the increase in funds for new research grants, provided in this bill, will permit some further expansion of this program. (Basic Biology of Venereal Disease) (Page 36 of House Report)	1. Grants support increased from three awards in 1970 to twenty-six in 1973, totaling $1,205,000. Grant awards in 1974 will be approximately $1,562,000.
1974 Senate Report	
2. During the past two years, Congress has urged the Institute to make greater efforts into the research of venereal disease, influenza and hepatitis. (Page 50 of Senate Report)	2. The Institute's 1974 level of research support for venereal diseases is estimated to be $1,562,000 as compared to $455,000 in 1972. For influenza research, approximately $3,040,000 as compared to $2,271,000 in 1972. For hepatitis research, the 1974 level of support is estimated at $2,315,000 as compared to $709,000 in 1972.

Authorizing Legislation

Legislation	1975 Authorization	1975 Appropriation Requested
Public Health Service Act Section 301--Research and Investigation, in general.	Indefinite	
Title IV, Part D--National Institute of Allergy and Infectious Diseases.	Indefinite	$110,404,000

NATIONAL INSTITUTES OF HEALTH

National Institute of Allergy and Infectious Diseases

Appropriations History

Year	Budget Estimate To Congress	House Allowance	Senate Allowance	Appropriation
1965	65,465,000	66,965,000	66,673,000	66,373,000
1966	71,247,000	71,247,000	73,816,000	74,194,000
1967	81,147,000	84,094,000	86,094,000	86,094,000
1968	89,097,000	89,097,000	92,190,000	89,081,000
1969	93,273,000	89,830,000	93,830,000	91,551,500
1970	96,500,000	96,500,000	98,991,000	97,805,500
1971	94,822,000	96,495,000	96,995,000	96,495,000
1972	94,848,000	101,513,000	107,233,000	103,600,500
1973*	95,697,000	107,730,000	129,316,000	107,730,000*
1974**	98,750,000	112,801,000	114,057,000	114,057,000**
1975	110,404,000			

* Note: This appropriation authority was the continuing resolution. The appropriation amount was the House Allowance, which was the lower of the House or Senate amounts in the first vetoed bill.

** Note: Appropriation after reduction, $110,461,000.

Justification

National Institute of Allergy and Infectious Diseases

	1974 Base*		1975 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits..........	596	$11,690,000	596	$12,135,000	---	+$445,000
Other expenses.........	---	98,771,000	---	98,269,000	---	-502,000
Total............	596	110,461,000	596	110,404,000	---	-57,000

General Statement

The Institute conducts and supports broadly based research on the causes, characteristics, prevention, control and treatment of a wide variety of diseases attributable to infectious agents (including bacteria, fungi, viruses and parasites) or to abnormalities or inappropriate responses of the body's immune mechanisms, such as allergies.

The Institute's entire spectrum of activities is subsumed under six main headings variously called Activities, Programs or Program Budget Activities.

In its attack on infectious and immunologic diseases the Institute strives: 1) to recognize and define a set of the more important national public health problems whose solution would be helped by increased research effort and 2) to decide upon the nature and extent of federal intervention in the research process judged most likely to expedite the finding of a solution.

The more important problem areas amenable to federal intervention are called Subactivities or Subprograms. Currently seven of these warrant a relatively high degree of intervention as characterized by including a collaborative, contract financed, institute coordinated component, one or more portfolios of highly relevant grant supported projects under the direct cognizance of institute staff, a structured communications activity for exchange of data, and a formal apparatus for scientific review and evaluation of portions of the program on a programmatic basis. The collaborative contracts component is conducted in partnership with industry, university research centers, other institutes and federal agencies. Currently there are nine other Subactivities or Subprograms which seem more wisely encouraged by a lesser degree of intervention. These are characterized by a portfolio of highly relevant, grant supported projects under the direct cognizance of staff, occasional workshops and provision for review and evaluation against program goals every three or four years.

The Institute also supports a large body of free ranging investigator-inspired research and the appropriate research training.

*Excludes 1973 appropriation restorations.

DHEW - National Institutes of Health

CROSSWALK - 1974 Column of 1975 Budget
(Dollars in thousands)

INSTITUTE: National Institute of Allergy and Infectious Diseases

Mechanism / Program	Research Grants Regular program	Research Grants Special programs	Training Programs Grants	Training Programs Fellowships	Laboratory and Clinical Research	Research and Development Contracts	Other Direct Operations	Total
Allergic & immunologic	21,671	1,172	1,480	894	---	2,541	---	27,758
Bacterial & fungal	18,029	1,153	1,650	873	---	2,236	---	23,941
Viral	13,945	1,249	836	393	---	5,378	---	21,801
Parasitic	8,076	1,010	558	309	---	625	---	10,578
Intramural	---	---	---	---	20,479	---	---	20,479
Res. mgmt. & prog. ser.	---	---	---	---	---	---	5,904	5,904
Mgmt. fund	---	---	---	---	(6,779)	---	(1,326)	(8,105)
Subtotal, base	61,721 1/	4,584	4,524	2,469	20,479	10,780	5,904	110,461
Program								
Allergic & immunologic	541	---	641	459	---	106	---	1,747
Bacterial & fungal	711	---	1,118	400	---	850	---	3,079
Viral	312	---	820	305	---	106	---	1,543
Parasitic	179	---	22	19	---	---	---	220
Subtotal, 1973 released	1,743 2/	---	2,601	1,183	---	1,062	---	6,589
Grand Total	63,464 3/	4,584	7,125	3,652	20,479	11,842	5,904	117,050

1/ Consists of $43,166,000 Non-competing grants and $18,555,000 Competing grants
2/ Competing grants only
3/ Consists of $43,166,000 Non-competing grants and $20,298,000 Competing grants

DHEW - National Institutes of Health

CROSSWALK - 1975 Column of 1975 Budget
(Dollars in thousands)

INSTITUTE: National Institute of Allergy and Infectious Diseases

Mechanism	Research Grants		Training Programs		Laboratory and Clinical	Research and Development	Other Direct	
Program	Regular program	Special programs	Grants	Fellowships	Research	Contracts	Operations	Total
Allergic & immunologic	20,777	1,411	1,407	1,523	---	2,100	---	27,218
Bacterial & fungal	15,498	1,225	1,569	1,500	---	4,200	---	23,992
Viral	13,299	1,243	795	1,015	---	5,536	---	21,888
Parasitic	7,116	1,015	530	621	---	500	---	9,782
Intramural	---	---	---	---	21,562	---	---	21,562
Res. mgmt. & prog. ser.	---	---	---	---	---	---	5,962	5,962
Mgmt. fund	---	---	---	---	(7,083)	---	(1,372)	(8,455)
Totals	56,690[1]	4,894	4,301	4,659	21,562	12,336	5,962	110,404

[1] Consists of $44,318,000 Non-competing grants and $12,372,000 Competing grants

Budget Mechanism

	1974		1975	
	Number	Amount	Number	Amount
Grants				
Regular				
Non-competing..............	820	$43,166,000	736	$44,318,000
Competing................	133	9,285,000	84	5,262,000
New.....................	133	8,916,000	108	6,830,000
Supplemental............	(19)	354,000	(15)	280,000
Subtotal..............	1,086	61,721,000	928	56,690,000
Special				
Scientific evaluation.....	---	150,000	---	176,000
International centers for medical research........	4	2,399,000	4	2,399,000
Research career program...	81	2,035,000	93	2,319,000
Subtotal..............	85	4,584,000	97	4,894,000
Total Grants................	1,171	66,305,000	1,025	61,584,000
Fellowships				
Non-competing..............	12	95,000	122	1,899,000
Competing.................	---	---	---	---
New......................	103	2,374,000	137	2,760,000
Supplemental..............	---	---	---	---
Subtotal................	115	2,469,000	259	4,659,000
Training Grants				
Non-competing..............	75	4,284,000	56	4,301,000
Competing.................	3	200,000	---	---
New......................	1	40,000	---	---
Supplemental..............	---	---	---	---
Subtotal................	79	4,524,000	56	4,301,000
Laboratory & clinical research	---	20,479,000	---	21,562,000
Research & development contracts.................	124	10,780,000	136	12,336,000
Research management & program services.................	---	5,904,000	---	5,962,000
TOTAL......................		110,461,000		110,404,000

Allergic and Immunologic Diseases

Authorizing Legislation:	Public Health Service Act, Title IV, Part D					
	1974 Base*		1975 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits..........	---	---	---	---	---	---
Other expenses..........	---	$27,758,000	---	$27,218,000	---	-$540,000
Total.........	---	27,758,000	---	27,218,000	---	-540,000
Subactivities:						
Asthma and Allergic Disease Centers.....	---	3,489,000	---	4,022,000	---	+533,000
Clinical Immunology...	---	7,293,000	---	7,703,000	---	+410,000
Total.........	---	10,782,000	---	11,725,000	---	+943,000
Budget Mechanism:						
Research Grants:						
Regular.............	---	21,671,000	---	20,777,000	---	-894,000
Special.............	---	1,172,000	---	1,411,000	---	+239,000
Subtotal..........	---	22,843,000	---	22,188,000	---	-655,000
Fellowships...........	---	894,000	---	1,523,000	---	+629,000
Training Grants.......	---	1,480,000	---	1,407,000	---	-73,000
Research & Development Contracts...........	---	2,541,000	---	2,100,000	---	-441,000
Total.........	---	27,758,000	---	27,218,000	---	-540,000

*Excludes 1973 appropriation restorations.

Introduction:

The most rapidly developing activity in the Institute's program is research on allergy and immunology. Basic science technology has developed methods of studying the body's responses to infections, to transplantation of organs, and to a variety of insect, food or plant pollen allergies. Scientists can now grow in the laboratory the cells involved in the immune response and do controlled and manipulative studies of the immune system which were impossible in the past. These studies will provide the basis for new therapy and for new diagnostic procedures. The asthma, allergy and clinical immunology subactivities are supplemented by regular research projects in the investigator initiated programs of the Institute. These investigator initiated programs utilize the disciplines of, genetics, molecular biology, biochemistry and cell biology. They are concerned with both immediate hypersensitivity and the longer range delayed immune responses of the body.

Asthma and Allergic Disease Centers:

Basic studies in immunology, long supported by the Institute, have provided findings which have opened the way for further studies designed to apply new knowledge to the benefit of the allergic patient. The Asthma and Allergic Disease Center subactivity is designed to speed this transaction of research into better health care.

Following the plans developed at the program's inception in 1971 the Institute continued to specially earmark funds in 1972 and 1973 for this program. During 1975 the Institute will continue to review applications for new centers but plans are for only modest expansion of the Center program. Enlargement of a few of the best Centers will be considered mainly through project awards in immediate hypersensitivity research and through the Allergic Disease Academic Award---a five year award designed to attract promising young investigators into academic allergy and launch them on a research career in this field. The coordination of plans and programs through meetings of the Center Directors will continue. The Institute is presently funding 17 Asthma and Allergic Disease Centers in 13 States at an amount of approximately $3,489,000. These centers in their short existence have demonstrated productivity and evidence of encouraging accomplishments. For example, the bronchial inhalation challenge, a diagnostic test for bronchial asthma, has been found to be a useful means of distinguishing allergic asthmatics among a total group of asthmatics with a positive skin test, thus enabling physicians to select patients most suitable for immunotherapy. In preliminary trials an antibiotic, troleandomycin, or TAO, has been shown to provide relief for some steriod-dependent asthmatics. It has been demonstrated that patients sensitive to honey bees are usually not sensitive to the stings of yellow jackets, hornets, and wasps, and vice versa. In another study to find out more about the interaction of cells via chemical mediators, a radioimmunoassay was used to measure cyclic AMP---a chemical substance that has recently been recognized to play a pervasive and critical role in the control of many cell processes. Cells from asthmatic subjects have been shown to have a significant decrease in their cyclic AMP response to beta-adrenergic drugs such as isuprel, norepinephrine and epinephrine in comparison with normal control cells. This alteration in responsiveness was most marked at the time of severe, active asthma, and returned towards normal during periods of clinical improvement.

The use of ragweed antigen E., polymerized to make a larger molecule by treatment with a chemical, glutaraldehyde, is being compared with conventional ragweed antigens for desensitization in one Center. Another Center is attempting to purify the central crystalline core of the granules of eosinophils, the white blood cells that increase in allergic reactions. Work is well underway at an Asthma Center in the collection, storage and subsequent computer analysis of clinical and biochemical data concerning children with intractable asthma. A continuing study of the effect of a chemical, trans AMCHA, on patients with hereditary angioedema has shown striking amelioration of the severity of the disease in 11 of 12 patients. Another Center is using amino caproic acid, a related drug, on such patients. The success of these drugs emphasizes the desirability of knowing the precise sequence of biological and chemical events that leads to symptoms of a disease and of understanding the mechanisms involved. The precise point at which both drugs interfere with the sequence is known and for the latter drug the mechanism seems reasonably well established. The recent licensing for use in the United States of Cromolyn (Intal), a potent anti-asthmatic drug, opens wide vistas for clinical trials using this drug, heretofore available only in European countries and Canada.

The Institute encourages effective collaboration among these Centers and integration of related research efforts by sponsoring annual meetings of the Center Directors and their key staff in Washington. The Inhalation Challenge Standardization Study Group has been formed from the scientists of the Centers to establish uniform methods of inhalation challenge, use of allergenic extracts and skin testing. A manuscript is in preparation delineating these proposed standards.

Clinical Immunology:

The ascendency of basic science research in immunology so visibly productive during recent years is now being matched by the direct application of experimental findings to allergy, autoimmune and immune complex diseases, chronic infections and leukemia representing a spectrum of human illnesses whose diverse natures had previously been either unknown or incompletely understood. As a result, there is increasing recognition and clarification of the pathologic changes in those organs or tissues that are responsible for maintaining and regulating functional integrity of the immune system and the circumstances under which immune processes can be manipulated in the treatment of underlying disease. This expanding scope requires especial expertise on the part of the immunopathologist dealing with the laboratory study of immunologically related mechanisms of disease and the clinical immunologist concerned with measures for diagnosis, control and treatment.

The lymphocyte biology program stands out as one area of basic research providing definitive and useful information pertinent to the needs of clinical immunology. Experimental data point to the characterization of the lymphocyte as the one blood and tissue cell playing the key role in initiating and regulating reactions of immunity. Accumulation of in-depth knowledge of its genesis, cellular functions and involvements is finding application in the understanding and management of a variety of diseases where immune-related lymphocyte derangements are being demonstrated.

The ability to identify lymphocyte types as derived from either the thymus gland (T cells) or the bone marrow (B cells) by their surface membrane markers and behavior in culture material has led to the finding that specific immune deficiencies are associated with the causes of some types of leukemia, neoplastic processes (Hodgkins Disease, lymphoid tumors), diseases of connective tissue (systemic lupus erythermatosus, scleroderma), and thyroid gland involvement. Other more familiar problem areas relating to lack of immune competence in patients suffering from uncontrolled chronic and recurrent infections can now be more specifically classified. As the specific nature of the immune deficiency becomes defined and recognized support will be given to work attempting reconstitution of functional immunity by implants of thymus gland or bone marrow.

The work of the clinical immunologist now dealing with patients afflicted by leukemia, lymphomatous tumors, cancer, intractable infections and other immune deficiency-related processes is being aided by the contributions of genetics research. Here, as in organ transplantations (e.g. skin grafts, replacements of diseased heart and kidney), the success of immune manipulations depends, in part, upon development of insights into the genetic factors that make for compatibility between implanted donor and recipient tissues.

Recognition of critical criteria to demonstrate competence or deficiency of the immune system has led to a change in our concepts of autoimmune disease (e.g. thyroiditis, pernicious anemia, lupus erythematatosus) in which the affected develops a reaction against his own tissues. With the emerging knowledge that the mechanism for recognition of changes in body tissue as "foreign" is identical to that for recognition of infecting microorganisms, work is underway to improve treatment of autoimmune diseases and cancer by immunologic techniques. These should replace the currently used cytotoxic drugs that have potentially deleterious side effects.

Important advances have been made in the recognition of distressing prpblems of infection in childhood responsible for high infant mortality. Whereas these had been thought to relate only to failure of effective formation of humoral antibodies or the development of resistance to antibiotics, new investigative approaches suggest that these are genetic defects in the function of the polymorphonuclear leukocyte (a white blood cell) and in fractions of the blood serum factor complement. Studies are continuing so that the diminished ability of this cell to engulf and destroy invading bacteria can be compensated.

An especially noteworthy development has been the first sign of success in the treatment of such chronic infections as leprosy, tuberculosis and those due to yeast and fungus organisms by the administration of a secretory product of the lymphocyte known as transfer factor. This experimental lead gives justified reason to focus in on research designed to determine the precise chemical nature of this material, to conduct treatment trials on patients with cellular immunologic defects, and to ascertain whether there are feasible production methods for recovery of transfer factor from large numbers of blood donors.

Since blood antibodies play such a vital role in defense mechanisms appreciation of the importance of the unraveling of the precise chemical makeup of one type of antibody - immunoglobulin G (IgG) - is evidenced by a Nobel Prize award to an Institute grantee. Similar work has resulted in the very recent definition of immunoglobulin M (IgM) and this provides encouragement to other investigators studying the chemistry of other immunoglobulin classes (IgA, IgE, IgD) and their overproduction in the invariably fatal disease, multiple myeloma.

Other antibody-related studies have revealed an "overshooting" aspect of the immune response. Overproduction of antibody by a defect in regulatory control or persistent stimulation (provided by microorganisms in chronic infection or by hyperimmunization) results in the formation and circulation of large amounts of aggregated protein masses (antigen-antibody complexes). In turn, their natural elimination via deposition in such vital organs as the kidney and lung has now been demonstrated as causative factors in immune complex disease processes. The pathogenesis of glomerulonephritis and hypersensitivity pneumonitis, triggered by streptococcal infection and inhalation of fungal spores from moldy hay respectively, emphasize the need to find ways of decreasing antibody response (e.g. immunologic tolerance) in situations where the hazard from environment is otherwise difficult to control.

Current research has helped to clarify many of the problems of tissue inflammation and allergic manifestations that accompany immune reactions. These point to chemical mediators generated and released by the interaction of antigen with specific types of antibody rather than due to the effects of antigen-antibody combinations per se. With this information at hand, work can go forward to develop effective immunopharmacologic agents capable of inhibiting the formation or release of the responsible inflammatory mediator or its neutralization, as well as measures to induce body tolerance to stimuli inducing causative specific class of antibody.

The subactivity in clinical immunology represents the work of approximately 33 research projects and approximately 20 contracts. An important part of the

Clinical Immunology subactivity deals with organ transplantation. Much of this is supported by contracts designed to develop, evaluate and utilize immunologic techniques and reagents to facilitate organ transplant and to prevent or ameliorate diseases resulting from immunologic dysfunction.

Highest priority is now given to the clinical evaluation of histocompatibility matching in the selection of organs for transplantation. It is estimated that there are approximately 8,000 new cases per year of end stage kidney disease. It has also been estimated that there are approximately 7,000 - 8,000 individuals presently on hemodialysis who would benefit from transplant of a healthy kidney. Amendments to the Social Security Act now provide payments for kidney transplants as well as for those individuals on hemodialysis. With this possibility of increasing the number of transplants it is important that the best possible techniques and reagents be employed to evaluate the clinical usefulness of tissue matching. A coordinated study to accomplish this evaluation has been underway since 1972 and will require support over a five year period. The program will also continue its efforts in 1974 to improve the dependability and speed of tissue typing by improving the quality of reagents, the sensitivity and specificity of typing techniques and hopefully by being able to provide for even wider distribution of these scarce and expensive typing sera.

It is not always possible to obtain good matches in unrelated pairs of donor and recipient since there are a multiplicity of tissue antigens and only a limited number of donors available at any one time. For this reason there is a program to evaluate the use of antilymphocyte globulin (ALG) in suppressing organ rejection even in poorly matched donors and recipients.

Recognizing the limitations on tissue typing, the ability to find the ideal donor-recipient match, immunosuppressive drugs and ALS, the program is seeking to develop other immunologic techniques to circumvent the natural resistance of an individual to accept the tissues or organs of another person. There are several theoretical ways of accomplishing this--enhancement and tolerance. The latter can sometimes be induced by injections of antigens under special circumstances by which the body learns to treat them later as its own. Enhancement may occur by the attachment of antibodies on the surface of foreign antigens or organs, coating them in such a fashion that the body does not recognize and reject them as foreign.

Bacterial and Fungal Diseases

Authorizing Legislation: Public Health Service Act, Title IV, Part D

	1974 Base*		1975 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits..........	---	---	---	---	---	---
Other expenses..........	---	$23,941,000	---	$23,992,000	---	+$51,000
Total.........	---	23,941,000	---	23,992,000	---	+51,000
Subactivities:						
Venereal Diseases.....	---	1,562,000	---	2,670,000	---	+1,108,000
Diseases Preventable by Vaccines.........	---	5,560,000	---	5,325,000	---	-235,000
Total.........	---	7,122,000	---	7,995,000	---	+873,000
Budget Mechanism:						
Research Grants:						
Regular............	---	18,029,000	---	15,498,000	---	-2,531,000
Special............	---	1,153,000	---	1,225,000	---	+72,000
Subtotal..........	---	19,182,000	---	16,723,000	---	-2,459,000
Fellowships...........	---	873,000	---	1,500,000	---	+627,000
Training Grants.......	---	1,650,000	---	1,569,000	---	-81,000
Research & Development Contracts...........	---	2,236,000	---	4,200,000	---	+1,964,000
Total.........	---	23,941,000	---	23,992,000	---	+51,000

*Excludes 1973 appropriation restorations.

Introduction:

Infections, particularly bacterial infections, are becoming a frequent hazard to the aged, to the very young, to the hospitalized, and to those who must undergo therapy which depresses their immune system. While many of the infectious diseases have been controlled by vaccines or the familiar antibiotic therapy, the more adaptable bacteria not only change their relative infectivity through genetic modification but also alter their resistance to antibiotics. Fungal infections, both the common superficial ones of the skin and the life-threatening deep systemic infections, are difficult to control and cure.

All infections run through a sequence of events including dissemination of the agent from a source (often an infected patient or animal), entrance of that agent into a susceptible human and its subsequent growth, damage to the host by a variety of organism products and through a variety of mechanisms and finally (and hopefully) clearance of the organism from the host and healing. Observation and experimental manipulation of all these events are material for the laboratory and clinical researcher. Hence the Institute's support of research on a diverse range of subjects.

Additionally some problems of infection have sufficient importance and conceptual coherence that they lend themselves to special attention. Such areas may be designated Special Emphasis Programs and currently the Institute has Programs in resistance of bacteria to antibiotics, hospital associated infections and streptococcal infections and sequelae.

Venereal Diseases:

The National Institute of Allergy and Infectious Diseases has responsibility within the National Institutes of Health for developing and implementing a program on venereal disease research. Objectives of this program are to overcome the many gaps in our knowledge and to gain the information sorely needed for eventual control of this varied group of diseases causing the current wide spread epidemic.

An Institute workshop in July 1973 evaluated current VD research developments with particular emphasis on identifying research problems and needs that could be more suitably supported by contracts than by grants. In 1975 the contract mechanism will be used in an attempt to supply resources critical to more rapid research progress. One important aspect of the current VD research problems is the shortage of skilled, motivated clinicians and research workers. Federal intervention by means of training grants, institutional and individual fellowship awards will be initiated by the Institute in 1975. These programs will undoubtedly have an important impact on the manpower problem, and ultimately on control of the epidemic. Continuation of the VD research program will remain as one of the priority goals of the Institute for 1975. The momentum already established in this critical public health area warrants expansion if eventual curtailment and control of the epidemic is to be achieved.

The current venereal disease program of the NIAID supports approximately 26 research grants, totaling $1,562,000, and averaging about $61,000 per grant. Investigations range widely, from study of fundamental biological properties of the causal agents, to development of more specific and rapid diagnostic techniques, and to search for more rational therapy. In addition to the microbial agents causing gonorrhea and syphilis, the two most common of the sexually transmitted diseases, others are now characterized from a public health viewpoint as probably belonging to this group. Included are the chlamydiae (a kind of bacterium that can grow only within living cells) which are one likely cause of non gonococcal urethritis (NGU) and of a transmissible eye disease, and T-strain mycoplasmas (a kind of naked bacterium) also probably involved in NGU and strongly implicated in infertility problems and perinatal diseases. Among the viruses, genital herpesvirus, besides its frank venereal disease role, is possibly implicated

Tuberculosis is still a disease of importance in the United States. Continued research is needed because atypical mycobacteria not only are difficult to characterize and to distinguish from the old style true tuberculosis but are being seen more frequently as cause of lung disease and because antibiotic resistant strains pose an increasing problem. Contract supported research is being continued and directed towards isolation and identification of biologically active constituents of the tubercle bacillus, as well as, studies on immunity and hypersensitivity in tuberculosis directed toward an eventual vaccine and improved therapy.

Leprosy remains a problem within certain areas of the U.S. as well as worldwide. Research grants in this area are evenly distributed to support studies of cultivation of the organism, pharmacology, immunology and experimental chemotherapy. Contracts have been used in evaluating antileprotic drugs for therapy and for interruption of the transmission cycle by mass chemoprophylaxis. Another bacterial problem of worldwide interest is cholera. Research in this area is primarily directed at studying methods of immunization, pathogenesis, microbial properties, and treatment of both cholera and cholera-like diseases. A great deal of work has been performed on the development of a toxoid for vaccine purposes and it has reached the point where it is expected that a suitable vaccine preparation will be available for use in a field trial during 1974-1975.

Of major concern in the area of preventable bacterial infections are streptococcal diseases and their after effects. Every parent is all too aware of the problems of "strep throat" and the possible after effects such as rheumatic fever and glomerulonephritis. Research grants continue to emphasize an effort to better understand the problems involved in these diseases. Contracts are supporting the development of a purified M protein fraction of the streptococcal organism which might serve as a vaccine. If this approach should prove feasible it could revolutionize pediatric medicine in the treatment of "sore throats". The physician would no longer need to put individuals on antibiotic treatment as a precaution against the development of the crippling rheumatic fever while bacterial cultures are being taken.

In summary, the Institute has a strong commitment to the development of vaccines and their evaluation. In this important area of bacterial vaccines, three vaccines are either undergoing field trials or ready to be tested. Currently being field tested for effectiveness in preventing disease are those for pneumococcal penumonia, otitis media and mycoplasmal pneumonia. Vaccines ready for evaluation of effectiveness include those for meningitis, streptococcal disease and cholera. Continued efforts are being made for improved vaccines in tuberculosis, leprosy and also meningitis and streptococcal disease.

in cervical cancer. Cytomegalovirus is probably a sexually transmitted agent and causes perinatal disease problems of both mother and infant.

Among the recent grantee accomplishments in this program are studies showing that pili (hair-like structures) of virulent gonococci aid in resistance of the microorganism to the body's cellular defense mechanism. The pili also show attachment to sperm cells, thereby contributing to disease transmission. Another study has shown that antibiotic resistance of the gonococcus is determined by several independent, closely linked genes within the bacterial cell; this antibiotic resistance can be transferred from one microorganism to another, indicating the potential for the spreading of antibiotic resistance in this bacteria. An investigator on syphilis reports that serum antibodies offer no protection against the disease suggesting that the almost unexplored cellular mechanisms may be the key to syphilis immunity. Another grantee reports that the purified outer envelope of the syphilis organism is similar in chemical structure to the endotoxin of gram-negative bacteria, although envelope function is yet to be determined. Growth of the causal organism of syphilis outside a living host is yet to be accomplished--this is one of the chief technical impediments to more rapid progress and the eventual development of a potential vaccine for syphilis.

Diseases Preventable by Vaccines:

The advent of antibiotics has led to an unwarranted sense of security concerning bacterial infections. There are still many problems resulting from resistant organisms and from sequelae of bacterial diseases without effective treatment. Therefore the Institute is greatly concerned with prevention of bacterial disease through vaccine development. The diseases under study in this category include meningitis, otitis media, pneumonia due to pneumococci and mycoplasma, cholera, tuberculosis, leprosy, and streptococcal infections.

A vaccine for the prevention of bacterial (pneumococcal) pneumonia has been developed and currently is being field tested. It is expected that within the next two years there will be a product ready for licensure. This will be especially useful for the populations at highest risk, for example, the elderly and the Indians.

Meningitis remains a serious disease in both the newborn and the young adult. A trivalent vaccine has been developed which includes meningococcus group A and C and Hemophilus influenzae type b purified polysaccharides. Research is ongoing for the development of similar material for meningococcus group B. These antigens correspond to the major etiological agents of bacterial meningitis. The trivalent vaccine has been evaluated for safety and ability to produce antibodies in small numbers of pediatric volunteers and enough is known about the difficulties of proving efficacy to make clear that a very large and costly field trial will be required. These infections occur fairly regularly each year and also for inexplicable reasons in small and large epidemic waves. They are dreaded not only because of their high mortality but because of the great risk of permanent impairment to intellect, sensory organs and locomotion.

Otitis media is one of the leading causes of deafness, especially among the Indian population. A vaccine has been developed against the eight main antigenic types of pneumococcus that cause this disease and it will be tested in small field trials for efficacy. A vaccine specific for mycoplasmal pneumonia is also ready for field trial.

Well designed and monitored field trials are becoming increasingly expensive to mount, partly because of the increased awareness for protecting the rights of human subjects and partly because of a sense of heightened responsibility to get a statistically significant answer, positive or negative, from this type of research.

Viral Diseases

Authorizing Legislation: Public Health Service Act, Title IV, Part D

	1974 Base*		1975 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits..........	---	---	---	---	---	---
Other expenses..........	---	$21,801,000	---	$21,888,000	---	+$87,000
Total.........	---	21,801,000	---	21,888,000	---	+87,000
Subactivities:						
Influenza and Other Respiratory Diseases	---	3,040,000	---	3,710,000	---	+670,000
Hepatitis.............	---	2,315,000	---	2,600,000	---	+285,000
Antiviral Substances..	---	2,830,000	---	2,856,000	---	+26,000
Total.........	---	8,185,000	---	9,166,000	---	+981,000
Budget Mechanism:						
Research Grants:						
Regular.............	---	13,945,000	---	13,299,000	---	-646,000
Special.............	---	1,249,000	---	1,243,000	---	-6,000
Subtotal..........	---	15,194,000	---	14,542,000	---	-652,000
Fellowships...........	---	393,000	---	1,015,000	---	+622,000
Training Grants.......	---	836,000	---	795,000	---	-41,000
Research & Development Contracts...........	---	5,378,000	---	5,536,000	---	+158,000
Total.........	---	21,801,000	---	21,888,000	---	+87,000

*Excludes 1973 appropriation restorations.

Introduction:

A little reflection about the variety of symptoms and the frequency of episodes of that universal malady--"the common cold" leads to the quite correct feeling that the multiplicity of viral diseases are a major contribution to the feeling of ill health. What may not be so obvious is the enormity of the aggregate socioeconomic impact of such seemingly mild diseases, nor the importance of such lethal diseases as influenza; nor the subtle long term role probably played by known and unknown viruses in a series of chronic and degenerative diseases; nor the complicated and poorly understood mechanisms by which the body responds to virus infection and (generally) cures it; nor the intricate way in which viruses can invade body cells and combine viral genetic material with animal genetic material to create, quite literally, biological monsters such as cancers.

A wide range of research is supported exploring aspects of all these problems. As leads develop which have the promise of being translatable in better care they are frequently pursued independently or cooperatively with other Institutes having more specific categorical interest or they become the object of specific concern as in the case of the subactivities listed above.

The prompt and accurate diagnosis of disease and identification of the causative agent have always played an important role in the treatment and prevention of disease. Much of the success in bacterial and parasitic infections have depended upon this. In preparation for the day when clinically useful therapies for virus diseases become generally available, rather than an infrequent research possibility, the Institute is initiating a program of clinical virology. This will give special attention to development of the techniques for diagnosis and the training of personnel to use such techniques and to manage viral infections through better understanding of the mechanisms of injury to the body and mechanisms of body defense.

Influenza and Other Respiratory Diseases:

Influenza remains the major viral respiratory disease in terms of morbidity, demand on medical care facilities, physicians and medical costs. Influenza and pneumonia are the fourth leading cause of death in the U.S. in a non epidemic year and first among all diseases as a cause of sick days in bed. The direct and indirect costs of the 1968-69 Hong Kong pandemic are estimated at $3,200,000,000. Influenza epidemics are reflected in excess deaths mostly, but not entirely, involving persons over 50 years of age and those with some degree of heart disease, lung disease or other major disability. This role of influenza is often not recognized by the individual physician hence not relfected in death certifications. Anticipating another major variant of influenza A virus in the late 1970's with an accompanying worldwide pandemic, the NIAID has held a series of interagency and scientific meetings. These have reviewed new data and have sought to develop a coordinated national plan for more effective combat of the disease and to plan critical research on the origin and pathogenicity of variants of influenza A virus.

Immunity in man is related to past exposure to external proteins of the virus called coat proteins. Influenza A virus is unique in genetic structure and in its unusual capability of developing mutants differing from that of other viruses causing respiratory disease. Mutations in genes controlling the structure of the protein coat appear to be the mechanism by which the virus adapts to partially immune populations during interpandemic periods. The pandemics are associated with major gene changes, probably brought about by proclivity for recombination (cross breeding). It is quite possible the recombinants of human and animal strains are the source of these new variants to which the population is non-immune because the coat proteins are either new or have not been experienced for many decades.

The Institute supports a wide ranging program of influenza research through both grant and contract mechanisms.

Extramural Support of Influenza Research
(dollars in thousands)

	CONTRACTS		GRANTS		TOTAL	
	No.	Amt.	No.	Amt.	No.	Amt.
1973 (Actual)............	7	$694	7	$476	14	$1,170
1974 (Est.)..............	10	1,050	8	650	18	1,700
1975 (Est.)..............	13	1,700	11	750	24	2,450

Grant supported research is largely devoted to gaining a better understanding of the genetics, biochemical and physical structure, and host-virus defense mechanisms. Contracts are mostly devoted to development and testing new vaccines, to refining detection and diagnostic mechanisms, to epidemiology, and to provision of critical reagents for investigators. Additionally, contracts are used to support conferences and workshops devoted to assessment of information, rapid dissemination of new information and research planning.

In 1974 these activities will be continued by both mechanisms. Better data will be sought on the efficacy of inactivated, purified, high potency vaccines in high risk populations. Clinical studies on live attenuated influenza vaccines will be expanded, particularly on temperature sensitive mutant recombinants which have the promise of more rapid production of vaccines containing the variants of the new coat proteins and of greatly lowering the amount of vaccine needed per population unit.

A National Conference on Influenza will be held in the Spring of 1975 to present new data and discuss its significance to the understanding of influenza. This Conference will also afford the opportunity to examine the socioeconomic consequences of the disease, as well as, the obligations and roles of various government and private agencies, the medical profession and industry in education of both the health professions and the public in new or improved methods of control.

Progress on prevention of other respiratory diseases is almost at a stand-still since it has been found that conventional approaches to immunization cannot be utilized. Research in 1975 will be given more emphasis through the grants mechanism toward better information on the structure, antigenic composition, and properties of the responsible viruses, towards study of the mechanisms of host immunity effective in naturally occurring disease, and the effect of all these on transmission and epidemiology. The importance of these diseases in morbidity and medical costs demands continued attention but new information must be developed before they can be effectively combatted.

Extramural Support of Research on
Viral Respiratory Diseases Other Than Influenza
(dollars in thousands)

	CONTRACTS		GRANTS		TOTAL	
	No.	Amt.	No.	Amt.	No.	Amt.
1973 (Actual)...........	10	$1,032	7	$489	17	$1,521
1974 (Est.)..............	10	1,000	5	290	15	1,290
1975 (Est.)..............	9	950	3	250	12	1,200

Contracts will continue to be used for support of research targeted at exploring the potential of live attenuated vaccines, seeking new agents, and providing reagents.

Hepatitis:

The Institute's program on viral hepatitis is designed to develop and evaluate new knowledge on the infectious cause and nature of hepatitis and translate this information as rapidly as possible into tangible means of prevention of infection or amelioration of symptoms. Program goals include development of improved detection methods and vaccines.

In 1975 it is estimated that this subactivity will include 10 contracts for $1,500,000 and 15 grants for $1,000,000. Maximum utilization will be made of the established system of facilities and resources for improved methods of detection, for defining more clearly epidemiologic patterns of infection and the nature of the disease, and for the earliest steps in the development of vaccines for both hepatitis A and hepatitis B.

Specific plans for 1975 call for increased utilization of animal models in studying experimental infection and disease caused by hepatitis A and B viruses; greater efforts to cultivate the hepatitis viruses A and B in laboratory systems such as tissue culture and embryonated eggs; further characterization of the viruses and their antigens; preparation of pilot lots of purified, concentrated materials which can be used as the starting materials for diagnostic and research reagents and experimental vaccine; and, in collaboration with CDC and other agencies, better definition of the number of cases of hepatitis occurring each year leading to better estimates of the socioeconomic impact of the disease.

During the past years the program has concentrated on developing the resources and technology for exploiting new knowledge as it became available. This included an investment in selecting and establishing animal model systems, a test laboratory, a study center, patient populations for ultimate evaluation of vaccines and hyperimmune globulins, and reagents. These were complemented by a strong in-house research effort and an interagency agreement with the Atomic Energy Commission for using highly sophisticated biophysical and biochemical techniques in studying the suspected viruses of hepatitis A and B and their related antigens.

Toward the end of 1973 the Institute investments in basic research paid off with two important breakthroughs: a team of scientists representing NIH grantees, the jointly sponsored NIAID-AEC MAN laboratory and NIAID intramural scientists found strong evidence identifying the virus of hepatitis B and differentiating it from other virus related antigenic structures, and intramural scientists visualized and positively identified for the first time the elusive virus of hepatitis A. These discoveries, coming closely on one another, are critical to developing vaccines and improving laboratory techniques for detecting or diagnosing viral hepatitis. The improved techniques permit differentiating hepatitis A and hepatitis B and from other types as yet identified, but strongly suspected of accounting for a substantial percentage of cases clinically diagnosed as hepatitis but not identifiable as hepatitis A or B. Of immediate practical value, is the possibility for measuring potency of human gamma globulin now commonly used for prevention of hepatitis A in close contacts of infected individuals and in travelers to foreign endemic areas. In 1975 the scientific opportunities presented by these advances will be exploited as rapidly and intensively as is currently feasible.

Antiviral Substances:

The great diversity of virus types necessitates the consideration of alternate approaches in combating viral diseases. Antiviral chemotherapy has as yet made no great impact on therapeutics comparable with that achieved by antibacterial drugs. For example, the only drug available for use in cases of influenza at present is amantadine hydrochloride. Its antiviral activity is not great and is limited to preventing infection rather than curing it. There is a need for a much more effective drug against influenza and drugs active against the many types of upper respiratory infections caused by viruses. Progress in this field, will constitute the major challenge to antiviral chemotherapy in its second decade.

There are also special cases of virus infections in which an effective chemoprophylactic agent would be of great value, such as exposure to rubella during the first trimester of pregnancy in a woman who has not had rubella and has not been vaccinated against it. In still another instance, reactivation of cytomegalovirus infections may occur during treatment with immunosuppressive drugs and this might be prevented with one of the drugs which are effective against herpes virus infections.

Drug therapy in viral diseases will be assisted by the development of a rational approach to the synthesis of chemotherapeutic agents. This approach can only be fostered by fundamental studies of the virus-cell interaction and the way in which viruses grow and replicate. Equipped with this basic virological knowledge, investigators may then logically devise means of disrupting the growth of the virus at the most vulnerable points and with least damage to ongoing host cell processes.

Although the investigation of the underlying mechanisms of viral replication is being pursued actively by research workers in the area of bacterial viruses (bacteriophage), other workers supported by this Institute are studying this phenomenon in animal viruses such as fowlpox, pseudorabies, polyoma, influenza, adeno, vaccinia, reo, arbo, poliomyelitis, rhino, sindbis, and vesicular stomatitis viruses. The essential unity or similarity of biological processes makes the findings in bacteriophage research quickly and often directly applicable to animal and human viruses. The NIAID currently supports over 100 projects for about $3,000,000 in research generally related to the areas above.

Interest in specific antiviral substances has focused primarily on interferon and on substances that stimulate its production in man, particularly since interferon has a broad activity against most viruses and is a natural substance which can be produced by the body itself. The Institute supports approximately 14 contracts and 13 grants in the amount of $1,400,000 for research directly related to interferon. The research supported through the grant mechanism is concerned with the mechanism of action and host factors which mediate the response leading to a basic understanding as to how interferon inhibits viral growth, particularly at the molecular level. The contract-supported research utilizes this information toward direct application to man. The latter includes development of effective and economical methods of producing interferon, purification studies leading toward possible chemical synthesis and clinical studies.

Parasitic Diseases

Authorizing Legislation: Public Health Service Act, Title IV, Part D

	1974 Base*		1975 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits..........	---	---	---	---	---	---
Other expenses..........	---	$10,578,000	---	$9,782,000	---	-$796,000
Total.........	---	10,578,000	---	9,782,000	---	-796,000
Subactivities:						
Immunity to Parasites.	---	1,880,000	---	2,020,000	---	+140,000
Biological Regulation of Vectors..........	---	2,690,000	---	2,860,000	---	+170,000
Total.........	---	4,570,000	---	4,880,000	---	+310,000
Budget Mechanism:						
Research Grants:						
Regular.............	---	8,076,000	---	7,116,000	---	-960,000
Special.............	---	1,010,000	---	1,015,000	---	+5,000
Subtotal..........	---	9,086,000	---	8,131,000	---	-955,000
Fellowships...........	---	309,000	---	621,000	---	+312,000
Training Grants.......	---	558,000	---	530,000	---	-28,000
Research & Development Contracts...........	---	625,000	---	500,000	---	-125,000
Total.........	---	10,578,000	---	9,782,000	---	-796,000

*Excludes 1973 appropriation restorations.

Introduction:

The Institute will continue to place special emphasis on immunity to parasites and on the biological regulation of vectors of disease, with particular concern -- in both areas -- for those diseases which are of major world wide importance. This emphasis is justified in view of the promise which research offers in helping achieve the goals of developing more effective methods for controlling parasitic diseases which afflict man or are transmitted by vectors -- usually mosquitoes, ticks or snails. Currently between 40 and 50 per cent of the number of grants and the amount of grant funds in this activity are devoted to research in these areas.

The balance of the program supports work on existing or potential problems on parasites which serve as excellent laboratory models for the study of a variety of disease processes. As an example of this "miscellaneous" parasitic disease category, grantees have recently demonstrated significant foci of infection in certain western states of the tapeworm which in man causes the potentially serious "hydatid disease". In some communities, up to one-third of the dogs examined were found infected with the adult worms. Future studies will concentrate on the distribution and prevalence of the infection, the role of sheep and wild animals in maintaining the infection in nature, and the most effective approaches for controlling the infection in man, especially by treating infected dogs -- the primary source of infection for man.

In view of the dearth of information on the full impact, in both human and economic measures, of many public health problems -- and parasitic diseases in particular, one of our grantees has estimated the consequences of pre-natally acquired Toxoplasma infections. Based on current prevalence and population data, he calculated that of the approximately three million babies born each year in the U.S., 3,000 of them might be expected to have a pre-natally acquired infection. Then, on the basis of the results of studies in France, the consequences of these infections were estimated as follows:

Estimated Consequences of 3,000 Toxoplasmic Babies
Born in U.S. per Year (Based on an infection rate of
one per 1000 pregnancies with 3,000,000 deliveries per year)

Consequence	Number	%
Death	150-450 babies	5-15
Severe brain/eye damage	240-300 children	8-10
Moderate to severe visual handicaps	300-390 children	10-13
Asymptomatic at birth - Some develop retinochoroiditis as children or young adults	1,700-2,150 children	58-72

The annual health care and special education costs of children born in any one year with toxoplasmosis is estimated to be $31,000,000 to $41,000,000.

Immunity to Parasites:

It is only recently that significant progress has been made in the study of the immunity to parasites because of their great complexity in structure, developmental stages and (often) migration in the infected animal. Now that these features of many parasites and their relationships to their hosts are better understood, and with the application to parasitic infections of the exciting developments in immunology, effective control of parasitic infections by immunization now seems to be a realistic research goal. During the coming year, much of the work will be concentrated on further purification and characterization of antigens shown to stimulate immunity; investigations of the various mechanisms by which the host responds to these antigens to develop immunity; possible ways of enhancing this response; and the potentially harmful effect of the immune response itself to the host. This latter point emphasizes that while it may indeed be possible to produce effective vaccines against specific parasites, effective control by use of the vaccines may require intervention in the immune response to protect the host against its own defensive mechanisms.

These points emphasize not only the practical importance of further studies on immunity to parasites, but suggest what may be of greater ultimate value: the use of several of the parasite model systems for the study of fundamental problems whose principles may be broadly applicable to many infectious and noninfectious disease processes. (The size and structure make some parasites much better suited to the elucidation of complex host-parasite relationships than other classes or organisms.)

While much progress is being made in understanding the mechanisms of immunity in vertebrates, very little is known about immunity in the invertebrates -- the mechanisms of vector-parasite relations or the factors that determine, for example, why some mosquitoes are able to transmit a virus disease or worm and others, even of the same species, are not. Such studies could lead to new approaches in the control of economically important vector-borne diseases such as dengue fever, virus encephalitis and filariasis.

Biological Regulation of Vectors:

A number of widely-publicized factors centered about development of resistance to pesticide and environmental persistance of pesticides have combined to make research on the biological control of disease transmitters a matter of considerable urgency. Even though there is a rather long history of work on biological control of plant and animal parasites of agricultural and veterinary importance, with some striking accomplishments, research on biological control of disease transmitters is at a relatively young stage of development. Consequently, the work will continue to cover a broad spectrum of fundamental studies to identify and explore the most promising approaches for control of various vectors.

An essential requirement for any successful program for control of disease transmitters (whether by biological measures, application of specific pesticides, environmental manipulation or a combination of these in an integrated pest management program) is a thorough understanding of the biology and population dynamics of the vector. Therefore, studies of this type will continue to be an integral part of the research in this area. Furthermore, extensive studies of the immediate and long range environmental effects of any proposed biological control program must be made before wide-scale field applications are undertaken.

It is appropriate to emphasize that there will be support for more extensive studies of the morphology and biology of insect viruses in order to provide a better understanding of the potential consequences of their widespread use as biological control agents.

Intramural Laboratory and Clinical Research

Authorizing Legislation: Public Health Service Act, Title IV, Part D

	1974 Base*		1975 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits..........	479	$9,352,000	479	$9,769,000	---	+$417,000
Other expenses..........	---	11,127,000	---	11,793,000	---	+666,000
Total..........	479	20,479,000	479	21,562,000	---	+1,083,000

*Excludes 1973 appropriation restorations.

Introduction:

Laboratory scientists based at Bethesda, Md. and the Rocky Mountain Laboratory, Hamilton, Montana, conduct a broad program effort for the discovery and exploitation of new knowledge aimed at the eventual prevention and cure of infections and diseases caused by abnormal immune reactions. Emphasis is on longer range problems difficult to accomplish under the research grant mechanism.

The intramural scientific program constitutes a vital bridge between the vast multidisciplinary biomedical research effort carried out in other institutions throughout the world and the applied research and technical development efforts represented in the Institute's Collaborative Research Programs. Collaborative (contract) programs such as those on respiratory virus vaccines and hepatitis often originate in intramural laboratories and those investigators may continue in a partnership by acting as technical advisors and project officers on contract projects.

Research results are transmitted to the biomedical community in the more than 300 scientific papers published annually and by presentations at national and international meetings, invitational seminars and workshops.

Allergic and Immunologic Diseases:

Clinical research in asthma and allergy began in 1973 when a well trained physician-scientist was recruited to initiate an asthma and allergic diseases center within the Laboratory of Clinical Investigation. By redistribution of resources it has been possible to expand this center slowly. It is now actively engaged in studies on urticaria (hives) and the biomedical mediators and immune apparatus involved in angioedema. Studies on asthma and on sensitivities (idiosyncratic reactions) to certain compounds used in x-ray studies have also been initiated. These clinical studies are coupled with laboratory research on the chemical and biological characteristics of the substances (mediators) that play an important role in the complicated interactions between cells at the time of a hypersensitivity reaction.

In 1975 the Asthma and Allergy Clinical Research Center will be moderately expanded to capitalize on a large outpatient population availability. Other studies in immunology will be continued at almost their present level. Efforts will also be made to evaluate the usefulness of transfer factor in coordinated controled clinical trials in such disease as chronic mucocutaneous candidiasis where defective cellular immunity is a major factor.

Major opportunities lie in research related to inborn immune defects and their correction, in the selective ability to stimulate or depress immunity to specific antigens, in the development of synthetic antigens (for instance, the coat antigens of a virus that are related to immunity to that virus), in correction of autoimmune diseases such as lupus erythematosus and nephritis, and in the capabilities of transplants between genetically different individuals. A rapidly burgeoning field of knowledge will lead to new methods of diagnosis, treatment, and prevention through emphasis on clinical immunology.

Clinical immunology research exploits the newly developed capabilities to alter immune processes. The use of transfer factor to correct the defective cellular immune process in certain fungal diseases is an example.

In 1974 a total of 54 senior scientists (21% of total) are engaged full time on research on allergy and immunology.

Bacterial and Fungal Diseases:

The Institute is one of the few centers in the United States where a specific program for research on the prevention, diagnosis and treatment of systemic mycotic infections is maintained. As more potent drugs are used in cancer chemotherapy, transplantation and the treatment of certain other diseases, fungi have become important causes of infection and death in such patients. Research on fungi ranges from studies on the genetics of pathogenic fungi for man to screening of new drug therapies in controlled trials.

Pseudomonas pneumonia is a severe, antibiotic resistant complication of immunosuppression, burns, and cancer chemotherapy. It is caused by a bacterium Pseudomonas aeruginosa which generally does not infect normal people. Research on the roles of the pulmonary macrophages, local immunity and humoral immunity has indicated that the macrophages and local immunity are more important in protection or recovery than is humoral immunity.

Streptococcal infections remain one of the most common and serious infections in populations because of rheumatic fever and other complications. Intramural research has concentrated on the "M" or protein antigen responsible for type specific immunity: on how it is formed, on recovery in purified form for biochemical and immunological characterization, and on the role of bacteriophages in the genetics of streptococci. While the research is mostly non-clinical, it underlies the effort to achieve better methods for control of these infections through immunity and to develop a capability of preventing the late after effects of rheumatic fever and nephritis.

Tuberculosis also remains an important national health problem and research continues on isolation and identification of the antigenic components of the cell wall of Mycobacterium tuberculosis which are responsible for immunity. Isolated components are characterized both biochemically and biologically. Components have been isolated which, when recombined with the cell wall skeleton, provide good immunity in experimental animals. These components are of considerable interest to the National Cancer Institute because they are superior to BCG in the suppression of experimental tumors. Work is continuing with partial support from NCI.

Endotoxic shock is a cause of major illness and death in burn patients, severely traumatized accident victims, transplant patients escaping control of immune rejection, and in severe gram negative bacterial infections. Endotoxin is also the component related to their capacity of many bacteria to induce fever and other physiologic effects. Institute scientists continue their research on the nature and properties of endotoxin, methods for induction of tolerance, and possible medical uses. Twenty-seven senior scientists (14% of total) are engaged in these studies.

Viral Diseases:

The largest commitment in intramural research is in virus diseases since these constitute the single greatest unsolved health problem of the American public. A total of 77 senior scientists (40% of total) are engaged full time in virological research ranging from vaccines for viral respiratory infections through antivirals to the very basic problem of integration of viral genetic material into host cells and the late effect of continued replication of these cells with altered genetic characteristics on the host.

Temperature sensitive mutants of influenza viruses capable of growing only in the upper respiratory tract have been developed and shown to be attenuated insofar as they can infect man without illness and produce immunity. The next problem is that of developing the capability to quickly transfer the temperature sensitive characteristics of laboratory made viruses to new variants. This capability would enable production of live attenuated virus vaccines quickly with one egg producing 100 to 1000 times the number of doses now possible with killed influenza virus vaccines. This work will be vigorously pursued in 1975 and is closely tied to contract activities for testing such mutants and their properties.

Viral hepatitis has become an exciting field after many years of frustrated efforts. Institute scientists have played a major role in developing new and highly sensitive test systems which have allowed more accurate screening of blood for hepatitis B infectivity, have developed animal models enabling beginning work on a vaccine against hepatitis B, and participated in research which clearly established the identity of the hepatitis B virus.

Acute viral infectious gastroenteritis ("winter vomiting disease," "intestinal flu") has been known for many years. Institute scientists during the last three years have isolated three separate viruses related to such outbreaks in various sections of the country and established them as a new family of viruses. Progress is hampered by the difficulty of growing these viruses in tissue cultures and experimental animals with the consequent necessity of using volunteers.

Institute scientists lead efforts to determine the potential role of interferon, a naturally occurring antiviral substance in man, in the prevention and treatment of human viral diseases. In collaboration with NCI scientists, they are also investigating the effects in certain types of cancer, since antitumor effects have been shown in experimental animals. An early problem was the fact that interferon inducers which were highly effective in animals were ineffective in man because man possesses an enzyme which quickly breaks inducers down. An Institute scientist seems to have circumvented this problem and his stabilized inducer will be tested during 1975 to determine its potentials and limitations. Other work involves interferon released from cell culture and mechanism of its action and possible use in various viral infections, particularly those that are life threatening or frequently accompanied by major disability (rabies, herpes viruses, encephalitis, and vaccina).

Other scientists are probing the mechanisms by which viruses enter host cells, reproduce, and produce either immediate death of the cell or long term genetic alterations. Inherent in these studies is the study of the cell products or other chemicals which can alter the virus activities and arrest its reproduction at various stages. Through this work studies are being made of specific biochemical products which have specific effects on the virus without alterations of the host cell and from such work we expect the eventual emergence of new antiviral chemicals. Perhaps more important is the study of how virus genetic material is incorporated into the host cell genetic apparatus so that the cell and all its future progeny, in effect, become new cells with differing morphological, physiological, and biochemical characteristics. While this is important to cancer research, it by no means is confined to cancer since it is suspected that many chronic and degenerative diseases such as certain central nervous system disorders, diabetes, arthritis, certain vascular diseases, and immune defects may stem from such altered cells. Latency of viruses is well known but not scientifically understood. The "slow virus diseases" lie somewhere in the fringe between other diseases and cancer, and there is growing evidence of the persistence of many viruses in noninfective states in the host for life after original infection. It cannot be overemphasized that these are long range problems with slow progress.

A major new need is establishment of a center where Phase I testing of new candidate vaccines can be carried out in volunteers. Past work has been done in prisons where volunteers were easily available and where participation did not create loss of income or other problems for the participant. Changes in prison systems have almost dried up this source and the Institute is seeking ways of recruiting college students as volunteers. Housing of such a center is not possible at NIH for lack of room in the Clinical Center at NIH and additional costs will be involved in contracting this out.

Parasitic Diseases (and Vector Borne Diseases):

Although lessened in emphasis over that given several years ago, the intramural program continues to be one of the few remaining centers for research on parasites and vector borne diseases connected with biomedical research in the United States. Research in parasitology has developed along two major lines--one, the more sophisticated study of the host parasite interactions including biochemical, immunological, and genetic parameters; the second, to explore the usefulness of such host parasite interactions as model systems in the study of other diseases, particularly allergy, cellular immune defects, and certain granulomatous diseases. Toxoplasmosis is a common and often serious parasitic disease in the United States causing eye disease and neonatal mental retardation. Institute scientists have played key roles in establishing the nature of this parasite, have shown that it multiplies in the intestine of the cat, and that the cat-rat complex may be important in its perpetuation and transmission to man. Americans living, stationed, or traveling abroad acquire parasitic diseases, among them malaria, amebiasis, schistosomiasis, trypanosomiasis, filariasis, and a variety of intestinal parasites. Little is known of immunity to these organisms or how it may be stimulated; diagnosis is often beyond most domestic laboratories and physicians, and treatment is far from optimum. Institute scientists study these parasites with an eventual goal of better prevention, or if this fails, better and more accurate diagnosis and effective treatment.

Tick borne diseases remain a threat as exemplified by Rocky Mountain Spotted Fever and Colorado Tick Fever. The Institute has the sole comprehensive capability in the United States for study of ticks and their disease associations. Scientists have worked actively with state and local health departments to develop a capability at those levels for the rapid detection of ticks infected with Rocky Mountain Spotted Fever rickettsia when these are removed from humans and the question is the likelihood of development of the disease. Other studies show that Colorado Tick Fever virus persists in the red blood cells of a victim of the disease for four to six months, thereby creating a hazard should the individual become a blood donor.

This work will continue at about the same level of effort in 1975. A total of twenty-seven senior scientists (14% of total) were engaged in parasitological research in 1974.

Funding of the major program areas reflects some change in emphasis but since the program is made up in large part of stable career scientists engaged in long range efforts, change must of necessity be slow. The funding by program is outlined below.

Funding Allocations for Intramural Laboratory and Clinical Research*
(dollars in thousands)

Program	1973 Actual	1974 Estimated	1975 Estimated
Allergy/Immunology	$3,371	$4,131	$4,355
Bacterial/Fungal Dis.	2,142	1,895	1,998
Virus Diseases	5,591	6,036	6,314
Parasitic & Vector Borne Dis.	1,862	1,638	1,812
Total	$12,966	$13,700	$14,479

* Excludes management fund

Research Management and Program Services

Authorizing Legislation: Public Health Service Act, Title IV, Part D

	1974 Base*		1975 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits..........	117	$2,338,000	117	$2,366,000	---	+$28,000
Other expenses..........	---	3,566,000	---	3,596,000	---	+30,000
Total.........	117	5,904,000	117	5,962,000	---	+58,000

*Excludes 1973 appropriation restorations.

These funds and positions provide for the overall coordination and administration of the Institute's grant and contract activity and staff assistance to the Institute Director for the planning, directing and administering of the grants, contracts and direct operations activities.

This program is responsible for planning and developing scientific programs for research and training grants, and fellowship awards. This involves the collection, processing, review and evaluation of applications, support of the National Advisory Allergy and Infectious Diseases Council, liaison with appropriate organizations and scientists, continual vigilance by professional staff of program progress on scientific activities and surveillance by supporting personnel on recording and reporting of varied information concerning grant management.

This activity also provides for the direction, planning, evaluation, administration, negotiation and award of the Research and Development Contracts program. It provides policy guidance, professional and technical assistance, evaluation of performance, maintenance of liaison with other Federal and non-Federal institutions, coordination and support of four operating units in conducting research in infectious diseases and immunology. It supplements and complements the intramural research programs. It also supports the various scientific advisory councils and boards associated with the various scientific activities, registries, workshops and meetings concerning the Research and Development Contracts program. In addition it provides for the overall administration, coordination and direction of all Institute research activities.

NATIONAL INSTITUTES OF HEALTH

National Institute of Allergy and Infectious Diseases

Program Purpose and Accomplishments

Activity: Allergic and Immunologic Diseases (PHS Act, Title IV, Part D)

1974		1975		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
---	$27,758,000	Indefinite	---	$27,218,000

Purpose: This program conducts and supports research and research training on a wide variety of diseases resulting from disorders of the body's complicated immune mechanisms.

Explanation: The program accomplishes its objectives through selection of research projects which are supported by research and center grants, fellowships and training awards and, where the state of the art permits, coordinated contract activities.

Accomplishments in 1974: There are three general long term objectives: to support high quality research via the grant mechanism in academic institutions; to encourage, by Federal intervention, increased research activity and communication on selected problems; and to initiate contract programs with sharply defined objectives.

Approximately 300 projects proposed by investigators were supported by grants, including 17 Asthma and Allergic Disease Centers, where laboratory-based immunologic research expertise is applied to clinical problems. Accomplishments included elucidation of the detailed structure of the antibody molecule by an investigator whose distinguished work won a Nobel prize award; increased knowledge of the mechanisms by which kidney disease in children is related to a series of immunological events; the laboratory development of two new ways of specifically suppressing deleterious immune responses (one of them dependent upon knowledge of the chemical structure of antibody referred to above).

Objectives for 1975: The Institute objective to reduce morbidity due to asthma and allergic disease will be managed through regular research projects and the coordinated efforts of the Asthma and Allergic Disease Centers. Plans are being made to expand clinical immunology and immunopathology research so as to benefit the patient whose immune system is depressed either through deficiencies of his own system, or secondary to other diseases or drugs.

The transplantation research contract program will study approximately 1,000 patients to determine the value of histocompatibility matching in organ transplantation. A standard protocol trial of antilymphocyte sera will be followed in approximately 100 patients to determine its value in sustaining transplanted kidneys (neither of the above studies will be completed in 1975). Studies to improve in quantity and quality the reagents available to perform typing for transplantation and transfusion will continue.

NATIONAL INSTITUTES OF HEALTH

National Institute of Allergy and Infectious Diseases

Program Purpose and Accomplishments

Activity: Bacterial and Fungal Diseases (PHS Act, Title IV, Part D)

1974		1975		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
---	$23,941,000	Indefinite	---	$23,992,000

Purpose: This program supports research and related research training on the causes, characteristics, mechanisms of disease production, prevention and control of diseases caused by bacteria, mycoplasma, fungi, including the toxic products of their growth or metabolism.

Explanation: The program is a carefully blended mix of activities supported by research and center grants in academic institutions, fellowships and training awards, and, where the state of the art permits, Federally initiated subprograms principally of coordinated and sharply focused contract activities.

Accomplishments in 1974: Approximately 385 projects were supported by grants. Examples of accomplishments from this investigator initiated research include: synthesis of the antibiotic fumagillin; exploration of the mechanism by which endotoxins cause shock through effects on the level of a complex substance (complement) in the blood; and the functional characterization of the mechanism by which leucocytes kill the fungus Candida. Infections with the latter organism are an increasing threat to patients treated with anticancer drugs.

Federal intervention occurred principally through Special Emphasis Programs, dealing with venereal disease, streptococcal infection, infections complicating hospitalization, and mechanisms of antibiotic resistance. An example of the accomplishments include the isolation and chemical characterization of tiny hair-like structures (pili) on the gonococcus and use of this knowledge in a new and sensitive diagnostic test.

The contracts programs include the following specific objectives: to develop, test and evaluate vaccines against bacterial pneumonia and meningitis; to assess the importance of histocompatibility matching for improving the success of renal transplantation; to evaluate a toxoid vaccine against cholera and to study certain facets of tuberculosis which might lead to an improved method of immunization.

Objectives for 1975: Grant support will give increased emphasis to infections complicating hospitalization and venereal disease. Attempts will be made to address research manpower shortages identified in venereal and fungal diseases.

In the contracts program it is planned to field test vaccines for bacterial pneumonia, meningitis and cholera; to initiate a research program for the ultimate control of venereal disease through improved detection and immunization methods; to continue the pharmacological studies of new drugs of potential value in treatment of leprosy and to evaluate the immunogenicity of streptococcal M. proteins prepared by different methods.

NATIONAL INSTITUTES OF HEALTH

National Institute of Allergy and Infectious Diseases

Program Purpose and Accomplishments

Activity: Viral Diseases (PHS Act, Title IV, Part D)

1974		1975		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
---	$21,801,000	Indefinite	---	$21,888,000

Purpose: This program is intended to permit the conduct and support of research and appropriate research training on the causes, characteristics, mechanisms of disease production, prevention and control of diseases believed to result directly or indirectly from viral or rickettsial infections.

Explanation: The program is a carefully considered mix of activities supported by research and center grants, fellowship and training awards, and, where the state of the art permits, Federally initiated subprograms principally of coordinated contract activities.

Accomplishments in 1974: Approximately 238 projects proposed by investigators were supported by grants. Examples of the accomplishments from this free ranging grant supported research include: the demonstration that a vaccine against one of the enzymes of the influenza virus will protect against the clinical disease even though it permits a mild infection to occur that engenders solid immunity against subsequent infection; and the laboratory demonstration that pandemic influenza strains may well arise by genetic recombination between human and animal influenza viruses.

Examples of the accomplishments of the contract activities follow. New candidate influenza vaccines were developed and tested in 1973 and 1974 and it appears that both temperature sensitive mutants (live virus) vaccines and neuraminidase-specific inactivated vaccines may have a useful and separate role in preventing influenza. Animal models have been developed for research and testing procedures for hepatitis B. Utilizing these models it appears possible that hepatitis B antigens, currently available in large quantity from human sources, could be inactivated and utilized for vaccines. New research reagents for hepatitis and influenza have facilitated both basic and applied research. Interferon and other promising antiviral drugs are now being tested in human trials.

Objectives for 1975: Research on influenza and other respiratory diseases will be emphasized.

The objectives of the contract program will be: to develop and initiate evaluation of a vaccine against hepatitis B and to identify and characterize the agent of hepatitis A; to test candidate vaccines for influenza, respiratory syncytial and parainfluenza virus; to study the feasibility of a dengue virus vaccine development project; to continue to evaluate promising antiviral drugs.

NATIONAL INSTITUTES OF HEALTH

National Institute of Allergy and Infectious Diseases

Program Purpose and Accomplishments

Activity: Parasitic Diseases (PHS Act, Title IV, Part D)

1974		1975		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
---	$10,578,000	Indefinite	---	$9,782,000

Purpose: This program is intended to permit the conduct and support of research and appropriate research training on the causes, characteristics, mechanisms of disease production, prevention and control of diseases produced or transmitted by parasites. Included are infections or infestations with a broad spectrum of infectious organisms (eg protozoa and worms) or arthropods (eg mosquitoes, flies, ticks).

Explanation: The program is a carefully considered mix of activities supported by research and center grants, fellowship and training awards, and, where the state of the art permits, Federally initiated subprograms principally of coordinated contract activities.

Accomplishments in 1974: It has been estimated that health care and special education costs of $31,000,000 to $40,000,000 would be required for the children born in the U.S. each year with toxoplasmosis. It has been shown that the infective stage of this parasite from cat feces can live in the soil for at least 15 months in the Kansas City area. Significant foci of infections of the tapeworm causing "hydatid disease" in man have been found in certain western states. In some areas, up to one-third of the dogs examined were infected with the adult worm.

Further progress has been made in studies which could lead to immunization against such important diseases as malaria, schistosomiasis and filariasis. The development of an anti-eosinophile serum by a grantee illustrates the value of parasite model systems for the study of the role of this cell in various disease processes.

Fundamental studies on mosquito genetics have led to development of genetic modifications of the mosquito Aedes aegypti which will be used in control field trials in East Africa this year in a program supported by U.S.A.I.D.

Contract activities provide required resources for research on schistosomiasis, filariasis and allergic hypersensitivity.

Objectives for 1975: Grant-supported research to develop the fundamental information required to achieve the long-range goals of effective prevention and control of parasitic diseases and control of disease vectors will be de-emphasized slightly. However, new initiatives will be undertaken as opportunities for their exploitation arise in such areas as further research on the unusual form of hydatid disease which occurs in Alaska and the mechanisms of immunity against disease organisms in vectors.

Further specialized manpower will be developed to achieve the goals of this program.

NATIONAL INSTITUTES OF HEALTH

National Institute of Allergy and Infectious Diseases

Program Purpose and Accomplishments

Activity: Intramural Laboratory and Clinical Research (PHS Act, Title IV, Part D)

1974			1975	
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
479	$20,479,000	Indefinite	479	$21,562,000

Purpose: This program supports highly qualified scientists to conduct investigations in immunologic and infectious diseases; to provide a source of expertise on specific projects to the collaborative (contracts) and extramural (grants) programs; to provide a resource under Federal control in the event of national medical emergencies; and to train physicians and other biomedical researchers.

Accomplishments in 1974: The long range objective of the program is the development of knowledge and technology leading to better prevention and control of infections and of immunologically mediated disorders such as allergy, asthma, and autoimmune diseases. Progress of the work is published in national scientific journals and taken together with the work of other scientists will eventually attain the objective of providing better solutions to health problems. In allergy and immunology, "transfer factor" is being evaluated in the correction of the deficient cellular immunity which underlies chronic candidiasis. Immunosuppressants are being investigated in several fatal or disabling granulomatous diseases, such as Wegener's granuloma. The Allergy Center began clinical research on urticaria ("hives") and asthma. Purified isolated antigenic components of BCG cell walls have been prepared and in collaboration with NCI scientists explored in tumor immunity. Efforts are being made to find better treatment for pulmonary infections with organisms such as Pseudomonas, a frequent cause of fatal pneumonia in immunologically compromised patients undergoing cancer chemotherapy. In virus diseases, there is a major effort on vaccine development against diseases caused by influenza, hepatitis and respiratory syncytial (RS) virus. New knowledge on viral genetics and mutagens has enabled exploration of live vaccines attenuated by introduced genetic defects. Preliminary human trials with such influenza, mycoplasma and RS virus vaccines have been completed with encouraging results. Collaboration between NIAID, CDC and the Bureau of Biologics has enabled development of sub-human primate models which in turn has allowed identification of the protective antigen of hepatitis B and provides a mechanism for study of this virus. A new technique of immune electron microscopy has permitted the first visualization of the viruses of hepatitis A and of epidemic gastroenteritis.

Objectives for 1975: To continue program with increased emphasis on better diagnosis and correction of immune disorders and on virus diseases, including antivirals and vaccines.

NATIONAL INSTITUTES OF HEALTH

National Institute of Allergy and Infectious Diseases

Program Purpose and Accomplishments

Activity: Research Management and Program Services (PHS Act, Title IV, Part D)

1974		1975		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
117	$5,904,000	Indefinite	117	$5,962,000

Purpose: This program provides for the over-all coordination and administration of the Institute's grants and contracts program, services rendered by the National Institutes of Health, and the support of the Institute's Director and his immediate staff in the overall administration, coordination and direction of all the Institute's activities.

Accomplishments in 1974: The established special emphasis programs were reviewed by the advisory council and staff for program content and adequacy of the dollar allocation used to provide preferential support of projects in these important areas. A new tentative dollar allocation for 1973 was established. A Task Force on Immunology and Disease became fully operational. It was divided into ten panels which conducted a survey of the entire field of immunology as it relates to the clinical process - disease. A scientific report was available in final draft form by the end of the fiscal year. The report will be given wide distribution in both scientific and a lay version, with the intent of developing a general appreciation of the importance of this discipline to all fields of medicine. Expectation is that it will become the base for detailed review by program advisory groups leading to recommendations for Institute action.

One Special Emphasis Program - Chronic and Degenerative Diseases of Man - was reviewed and evaluated by an ad hoc working group. The evaluation process covered program content, specific goals and objectives, progress towards accomplishment of those goals and objectives, relevance of proposed research to those goals, quality, program balance, and current importance of the research effort.

A special consultant was engaged to review and evaluate the extramural programs concerned with the viral diseases of man. A written report of progress was made as well as a presentation to the advisory council. A final report was made at the end of the fiscal year.

Another special consultant was engaged full-time for a portion of the year to review and evaluate the extramural allergic disease programs, particularly the size and nature of the problems encompassed by clinical allergy.

Objectives for 1975: This program will continue to support and improve management and coordination of Institute programs. Emphasis will be toward developing better scientific communication and the social and economic impact of special interest to NIAID.

THURSDAY, MARCH 28, 1974.

NATIONAL INSTITUTE OF GENERAL MEDICAL SCIENCES

WITNESSES

DR. LEO H. VON EULER, ACTING DIRECTOR

DR. ROBERT S. STONE, DIRECTOR, NATIONAL INSTITUTES OF HEALTH

DR. DeWITT STETTEN, JR., DEPUTY DIRECTOR FOR SCIENCE, NATIONAL INSTITUTES OF HEALTH

DR. ARTHUR E. HEMING, ASSOCIATE DIRECTOR FOR PROGRAM ACTIVITIES, NATIONAL INSTITUTE OF GENERAL MEDICAL SCIENCES

GORDON J. KLOVDAHL, EXECUTIVE OFFICER, NATIONAL INSTITUTE OF GENERAL MEDICAL SCIENCES

MRS. EMMA LOU AKERS, BUDGET OFFICER, NATIONAL INSTITUTE OF GENERAL MEDICAL SCIENCES

LEON M. SCHWARTZ, ASSOCIATE DIRECTOR FOR ADMINISTRATION, NATIONAL INSTITUTES OF HEALTH

LELAND B. MAY, ACTING DIRECTOR OF FINANCIAL MANAGEMENT, NATIONAL INSTITUTES OF HEALTH

CHARLES MILLER, DEPUTY ASSISTANT DIRECTOR, BUDGET

Object Classification (in thousands of dollars)

Identification code 09-25-0851-0-1-651		1973 actual	1974 est.	1975 est.
	Personnel compensation:			
11.1	Permanent positions	2,613	2,690	2,669
11.3	Positions other than permanent	49	81	81
11.5	Other personnel compensation	59	49	49
11.8	Special personal services payments	---------	---------	---------
	Total personnel compensation	2,721	2,820	2,799
12.1	Personnel benefits: Civilian	302	306	306
21.0	Travel and transportation of persons	124	163	163
22.0	Transportation of things	23	34	34
23.0	Rent, communications, and utilities	186	275	295
24.0	Printing and reproduction	90	140	140
25.0	Other services	6,706	9,063	7,034
26.0	Supplies and materials	48	68	69
31.0	Equipment	16	54	54
41.0	Grants, subsidies, and contributions	143,819	184,583	157,435
99.0	Total obligations	154,035	197,506	168,329

Personnel Summary

Total number of permanent positions	171	156	155
Full-time equivalent of other positions	5	5	5
Average paid employment	171	161	160
Average GS grade	8.5	8.6	8.6
Average GS salary	$14,260	$15,138	$15,473
Average salary of ungraded positions	$11,138	$12,018	$12,253

Program and Financing (in thousands of dollars)

	Identification code 09-25-0851-0-1-651	1973 actual	1974 est.	1975 est.
	Program by activities:			
	1. Pharmacology-toxicology	26,908	27,803	26,175
	2. Biomedical engineering	20,636	24,597	21,421
	3. Clinical and physiological sciences	22,479	25,953	23,251
	4. Genetics	48,162	50,024	46,087
	5. Cellular and molecular basis of disease	48,602	57,220	44,925
	6. Research management and program services	5,497	6,610	6,470
	7. General research support grants	2,583	5,299	
	Total program costs, funded [1]	174,867	197,506	168,329
	Change in selected resources (undelivered orders)	−20,832		
10	Total obligations	154,035	197,506	168,329
	Financing:			
25	Unobligated balance lapsing	29,177		
	Unobligated balance restored		−29,177	
	Budget authority	**183,212**	**168,329**	**168,329**
	Budget authority:			
40	Appropriation	183,171	176,778	168,329
	Withheld from obligation and expenditure (Public Law 93-192)		−8,449	
42	Transferred from other accounts	41		
43	**Appropriation (adjusted)**	**183,212**	**168,329**	**168,329**
	Relation of obligations to outlays:			
71	Obligations incurred, net	154,035	197,506	168,329
72	Obligated balance, start of year	123,057	106,513	106,504
74	Obligated balance, end of year	−106,513	−106,504	−66,328
77	Adjustments in expired accounts	262		
90	Outlays	170,841	197,515	208,505

[1] Includes capital outlays as follows: 1973, $16 thousand; 1974, $54 thousand; 1975, $54 thousand.

NOTES

Excludes $1,778 thousand in 1975 for activities transferred to (in thousands of dollars):

	1975
National Cancer Institute	326
National Heart and Lung Institute	420
National Institute of Dental Research	42
National Institute of Arthritis, Metabolism, and Digestive Diseases	300
National Institute of Neurological Diseases and Stroke	178
National Institute of Allergy and Infectious Diseases	176
National Institute of Child Health and Human Development	182
National Eye Institute	70
National Institute of Environmental Health Sciences	28
National Library of Medicine	12
Office of the Assistant Secretary for Health	44

Comparable amounts for 1973 ($1,524 thousand) and 1974 ($1,524 thousand) are included above.

WITNESS INTRODUCTION

Mr. FLOOD. We have the National Institute of General Medical Sciences and the presentation will be made by Dr. Leo H. von Euler, Acting Director.

We will insert your biographical sketch in the record.

[The biographical sketch follows:]

BIOGRAPHICAL SKETCH

Name: Leo Hans von Euler.

Position: Acting Director, National Institute of General Medical Sciences.

Birthplace and date: Stockholm, Sweden, January 31, 1931 [American citizenship, Oct. 5, 1954].

Education: B.A., Williams College, 1952, graduate study in biology, Tufts University, 1952–53, M.D., Yale University School of Medicine, 1959.

Experience: Acting Director, National Institute of General Medical Sciences, February 1974–present. Deputy Director, NIGMS, March 1974–present. Acting Director, clinical and phsiological sciences program, NIGMS, June 1973–present. Acting Deputy Director, November 1972–March 1974. Acting Associate Director for Manpower, NIGMS, June–October 1972. Chief, Medical Sciences Section, Research Training Grants Branch, NIGMS, 1969–72. Program Administrator, Research Training Grants Branch, NIGMS, 1967–69. Biochemist, Nutritional Biochemistry Section, National Institute of Arthritis and Metabolic Diseases, 1966–67, resident, clinical pathology, Clinical Center, NIH, 1963–66, research fellow, Department of Pharmacology, Yale University School of Medicine, 1961–63. Internship, residency, Yale-New Haven Medical Center, 1959–61. Research Assistant, Sterling-Winthrop Research Institute, 1955, U.S. Army, 1953–55.

Association memberships: American Society for Experimental Pathology, American Association of Pathologists and Bacteriologists.

Special awards, citations, or publications: Diplomate, American Board of Pathology in anatomic and clinical pathology, March 26, 1966.

Mr. FLOOD. Do you have anybody you want to introduce?

Dr. VON EULER. Yes, I do. On my left is Mr. Klovdahl, executive officer of the Institute. On my far left is Dr. Arthur Heming, associate director of program activities. Behind me is Mrs. Emma Lou Akers, budget officer.

Mr. FLOOD. You have a prepared statement, Doctor. How do you wish to proceed?

Dr. VON EULER. I would like to read it if I may.

Mr. FLOOD. You may proceed.

OPENING STATEMENT

Dr. VON EULER. Mr. Chairman and members of the committee, it is my privilege to appear before the committee to present some of the accomplishments and aspirations of the programs of the National Institute of General Medical Sciences. In an overall sense, this Institute seeks to foster the acquisition of knowledge that will be basic for developing better ways to maintain human health. Its programs support research and research training that extend from fundamental laboratory exploration to clinical research. An important program in the Institute is concerned with the development of better diagnostic and therapeutic instruments and their automation.

BIOMEDICAL ENGINEERING PROGRAM

The biomedical engineering program provides illustrations of the interesting and often unexpected interrelationships that may occur in science. During the Second World War, physical scientists developed an effective technology for underwater detection and localization of submarines through the reflection of sound waves. Sonar is now a household word. Through extension of this technology in ultrasonics into the biomedical area, engineers have developed methods for the measurement of blood flow and heart function which eliminate the hazards involved in invading a blood vessel, as with a needle or catheter. NIGMS-supported scientists are now developing ultrasonic blood flow mters for clinical application. Ultrasonic technology is also providing the diagnostic radiologist with a way to visualize soft tissues that avoids the dangers inherent in the use of X-rays or radioactive isotopes. Efforts are underway to develop ultrasonic camera systems which would give clear images of internal organs comparable in detail to pictures taken with an ordinary light camera. An instrument of this type is now nearing completion at the Stanford Research Institute, with support from the NIGMS.

CLINICAL AND PHYSIOLOGICAL SCIENCES PROGRAM

The Institute's program in clinical and physiological sciences includes the area of anesthesiology and trauma, in which the Congress has been extremely interested. During the past year, one of the Institute's grantees in this program, at the NIGMS Trauma Center in Dallas, has achieved a unique succss in the treatment of severe burns, which constitute a significant fraction of this country's trauma cases. He was able to save a young patient with a burn that covered 92 percent of her body. This success was attributed to: The rapid correction of fluid imbalances, the recognition and reversal of early anemia, and the accurate prediction of pending infection by the identification of antibodies from the tissue under the scab. In addition, the application of fresh, immunologically matched cadaver skin under hypotensive anesthesia has been highly successful. Using these advanced methods of treatment, this center has been able to lower the mortality rate for severe burns from 80 percent to 57 percent. Such reduced mortality rates also apply to smaller surface burns, as shown in the more than 3,000 patients treated at this center.

Looking at trauma from the opposite end of the spectrum, from the cellular point of view, one of our grantees has reported a highly provcative finding. This investigator has shown that the smooth muscle cells which comprise the main cellular element of atherosclerotic lesions were derived originally from a single cell in the vessel wall. The methodology for demonstrating this made use of several findings from the field of genetics; for example, the discovery that the gene for a particular enzyme or protein is transmitted by one of the sex chromosomes, and further that there are several different inherited varieties of this gene and enzyme. It was found that even in relatively large pieces of tissue from atherosclerotic lesions, the cells all contained the same variety of enzyme. This was not the case with tissue from normal vessel wall, implying strongly that the "atherosclerotic" cells are all the progency of a single cell. This cell must somehow have been stimulated to divide at an abnormal rate. If confirmed, this finding would have great implications with respect to the nature of the initiating event in the development of atherosclerosis, but the interpretations are still highly speculative. One such event might be the activation of a so-called slow virus. As with the work of so many of our grantees, this fundamental research on cell pathology has important implications for work being conducted by other institutes.

PHARMACOLOGY-TOXICOLOGY PROGRAM

Research in clinical pharmacology, sponsored by the pharmacology-toxicology program of the Institute, has demonstrated that the drug azaribine, which has not been released for general use, appears to be an effective form of therapy in severe psoriasis. This disease, the cause of which is unknown, varies in severity from extremely mild to severly incapacitating, and may result in death. Even in less severe cases, however, the disfiguring physical manifestations of the disease can be extremely damaging psychologically to affected individuals. The new drug has now been tested in over 400 patients with severe systemic psoriasis and psoriatic arthritis resistant to other therapy. A good to excellent therapeutic response was experienced by over 75 percent of these patients. Research is now directed at determining the risk of possible adverse reactions to the required doses of the drug and to seek methods which may be utilized to counter such adverse effects. Although the drug is still in an experimental stage of development, the potential usefulness of this drug or others like it is very great. They would have direct impact on the health and well-being of as many as 1½ million people who are estimated to suffer at one time or another from psoriasis severe enough to interfere with daily activities.

GENETICS PROGRAM

The Institute's genetics program is now supporting eight genetic research centers, of which one was initiated in the past year. Additional applications are being carefully reviewed, and we have two ready to be funded. A repository for a variety of human cell types at the Institute for Medical Research in Camden, N.J., is now in its second year of operation. Skin biopsies and other small pieces of tissues from individuals suffering different genetic diseases are collected, preserved, and made available to qualified investigators for study. During the first year of its support under a contract with the NIGMS, samples of some 160 cell types were shipped to investigators all over the country. The repository is being increasingly recognized as a national resource.

Several brief highlights of genetics research may be of special interest to the committee. Cystic fibrosis is the most common inherited disease in the white population, affecting one in 1,500 live births. The gene is so prevalent as to threaten the offspring of one in every 400 marriages. It has been known for some years that the blood serum from patients with cystic fibrosis, when applied to an isolated piece of rabbit windpipe, disturbs the normal rhythmic beating of the tiny, hairlike projections lining the inner surface of the windpipe. A similar effect can be observed under the microscope in certain tissues of the oyster, and with the aid of this test system, the chemical identity and structure of the active ingredient is now being sought.

Much of the basic research supported by this program concerns what might be called obligatory genetic diseases; that is, individuals with a particular genetic makeup manifest disease in all cases. Another group of genetic diseases only become apparent in special environments or following exposure to particular medication or environmental pollutants. An important instance of the later has recently been described by an Institute grantee working at the NIGMS Genetics Center in Houston. He has demonstrated that susceptibility to lung cancer is in part inherited. Some individuals react to chemicals in tobacco smoke and to other noxious substances by producing significant amounts of an enzyme, which converts these substances into active, cancer-causing forms. Other individuals react by producing only minor amounts of this enzyme and are consequently much less exposed to the risk of developing lung cancer. The hereditary pattern of reacting to these chemicals is straightforward, and the population divides itself into three groups. If both parents react to cigarette smoke by producing high levels of the enzyme, their offspring will react the same way; if neither parent reacts strongly, the offspring will not do so either; and, finally, if one of the parents is a strong reactor, the offspring will be intermediate, and be moderately susceptible to lung cancer. The grantee is currently perfecting a simple blood test to detect these genetic differences. With such a test, early precautions could be taken with regard to smoking or exposure to other cancer causing chemicals. This example emphasizes what is, in our opinion, a most important attribute of progress in the genetics program; namely, the relevance of this research to the prevention of disease as distinct from the cure of disease.

The genetics program as a whole raises a number of questions that need discussion and answers from society, as well as from the medical profession. I am referring to questions of medical ethics. It has seemed to us that in addition to scientific knowledge, ethical and moral sensitivity has become an essential ingredient, both in the medical laboratory and the clinic. The investigators in our genetics centers, especially, have expressed concern and interest in genetic counseling, which has to go hand-in-hand with clinical work in this field. At the present time, there are insufficient data on how effective these counseling efforts are, and scattered attempts to evaluate this work have been proposed and are, in a few cases, in process of being carried out. However, to be statistically valid, experience with greater numbers of patients than are usually seen at any one center are needed, and a coordinated effort is probably required to standardize the data collection and make it possible to pool the results. Toward this end, the Institute is moving to set up a conference of experts who could develop appropriate guidelines and establish the requirements of such a coordinated effort. Since its proper administration and evaluation will require considerable social science expertise, the major support might more appropriately come from another agency. We have approached the Health Services Administration, which is now considering the problem. The NIGMS, however, is interested in identifying the needs and cooperating in research aspects of the study.

The committee will be interested to learn that two of our most recent appointments to the National Advisory General Medical Sciences Council are highly informed and strongly committed lay members interested in health, basic research, and genetic diseases. Mr. Robert D. McCreery has been president of the National Cystic Fibrosis Foundation since 1969, and Mrs. Marjorie M. Guthrie was a founder of the Committee to Combat Huntington's Disease. To increase the public awareness of the challenges and problems of genetic disease, the Institute is publishing a fact sheet entitled: "What Are the Facts About Genetic Disease, Most Ubiquitous of All Human Maladies?

CELLULAR AND MOLECULAR BASIS OF DISEASE

We have all been much concerned recently with obtaining and distributing energy to heat our homes, move our goods and ourselves, and to keep our factories going. Analogously, many of the grantees in the cellular and molecular basis of disease program are doing fundamental research on the management of energy in the living body. It, too, of course, requires energy to maintain its 98.6 degrees, to move its muscles, and to carry out its many chemical reactions. We take these body processes for granted, until something goes wrong, as when we develop a fever, become hyperactive in thyroid disease, or convert too much energy to storage fat. These physical and chemical processes represent a molecular technology that has evolved in living systems oveu millions of years, and the study of them may not only be relevant to health, but could yield spin-off benefits in the search for solutions to our society's energy problems.

Let me say something briefly about the cell's power plants. No so long ago, the cell was regarded simply as an unstructured bag of cell sap and enzymes. Enzymes are the protein catalysts necessary if various chemical reactions are to proceed at the relatively low temperature of the human body. These chemical reactions are innumerable, ranging from the buildup of complex molecules to their ultimate breakdown into waste products. The development of the ultracentrifuge, the electron microscope, radioisotope methodologies, and sophisticated light-measuring instruments has revolutionized our understanding of cell structure and function. We now recognize that the cell is not simple at all, but a highly complex and well-organized system of structures with distinctive anatomical and functional features. These structures are referred to as organelles. Among them are the power plants of the cell, called mitochondria, which are small bodies residing in the cell fluid, or cytoplasm, outside the nucleus. The mitochondria contain the enzymes which transform energy released from foodstuffs, such as sugars, proteins, and fats, to a form that can be utilized in the cell for energy-requiring processes.

Mr. SMITH. In connection with this there have been some recent articles that lowering the temperature of the body extends life. Has that something to do with this?

Dr. VON EULER. It could have something to do with this.

Mr. SMITH. Has there been any research on that aspect?

Dr. VON EULER. Not specifically, no, sir. The adaptation of human beings to the cold in the environment we have been studying, but not the prolongation of life.

One increasingly important aspect of the cellular and molecular basis of disease program involves the study of what might be called the mitochondrial diseases; that is, diseases specifically involving these cell organelles. The layman and practicing physician alike usually describe and think of disease in terms of the most prominently affected body organs. We speak of heart disease, muscle wasting, cirrhosis of the liver, or degeneration of the nervous system. It is clear, however, that these gross manifestations are the results of derangements at a much finer level of organization, and that the changes in individual cells and their components may play the primary role in causing disease. Illustrative examples are the fatty livers and cirrhosis induced by alcohol consumption. In terms of clinical significance, liver damage from chronic alcohol abuse is the most important chemical injury to which man is exposed. In New York City, cirrhosis is the third leading cause of death between the ages of 25 and 65. Under the microscope fatty livers caused by chronic alcoholism show alterations in the structure of mitochondria, which appear enlarged and distorted, with disorientation of their inner folds. These changes are observed both in alcoholic humans and in rats fed experimentally, and are accompanied by impaired function of the mitochondria—for example, their ability to oxidize fatty acids and make the proteins that normally would carry the fats out of the liver.

Another well recognized clinical condition is thyrotoxicosis caused by overproduction of thyroid hormones. The excess hormone acts to speed up body metabolism and results in weakness, increased fatigue, weight loss, insomnia, sweating, and bulging eyes. Experimental evidence suggests that thyrotoxicosis is a disease of defective energy transfer, and it has been shown that thyroid hormones uncouple the consumption of oxygen from the production of usable energy. Mitochondria obtained from animals treated with thyroid hormone are swollen or more susceptible to swelling, but the details of how their function is impaired remain to be understood.

The list of disease conditions in which abnormalities in mitochondrial structure have been observed with the electron microscope is by now impressive, including various muscle diseases, diabetes, and shock. Abnormalities of mitochondria have also been seen after exposure to a long list of chemicals and drugs, and in old age, and interesting correlations are beginning to emerge between the functional and structural changes. In analogous fashion, other diseases are coming to be recognized that involve each of the dozen or more organelles that have been identified within cells. Many of these were completely unknown when the NIH extramural program was started in 1946.

In view of the central importance of mitochondria to the energy metabolism of nearly all living cells, it can be said that these tiny cellular organelles are as important to the life of each cell as the heart is to the human body, and that our understanding of the mitochondria and their altered structure and function in disease will be as important to medicine in the future as our understanding of the human heart is today.

Progress in all these programs is strongly dependent on new ideas, which means, ultimately, new young scientists. Without the proper regrowth, the creative yield of the academic departments, where most of this research is conducted, will diminish. In order to safeguard the high quality and preparation of the young scientists entering our research programs, and thus assuring the wisest possible expenditure of future Federal research dollars, the NIGMS has continued to provide grants-in-aid for research training leading to the Ph. D. degree.

Mr. Chairman, to support the efforts outlined above, the appropriation request for the National Institute of General Medical Sciences for 1975 totals $168,329,000, I shall be pleased to try to answer any questions and supply additional information desired for the record.

BUDGET REQUEST

Mr. Flood. Doctor, your budget request for fiscal year 1975 is at the same level as the 1974 adjusted appropriation, $168.3 million; is that right?

Dr. von Euler. That is right.

1973 IMPOUNDED FUNDS

Mr. Flood. In 1974 you received $29.2 million of restored 1973 funds.

Dr. von Euler. Yes.

Mr. Flood. In which program areas did you invest those funds?

Dr. von Euler. In all five of our programs.

Mr. Flood. Did you make any of these multiyear awards, two years or more, in fiscal 1974?

Dr. von Euler. Roughly $20 million of the total for 1974 has been assigned to multiyear awards.

Mr. Flood. In the record we want a revision of your justifications on page 15. We want you to insert a revision of the table. Specifically we want to see reflected in the 1974 column the restored funds we are talking about and in the 1975 column we want to see the impact, if there is any, of the action taken in 1974. Also, of course, be sure on the table that you have 1972 and 1973.

Also for the record a table for fiscal years 1973 through 1975 showing how much you have invested in each of the program areas.

[The information follows:]

Obligations by Budget Mechanism
Showing "True" Program Levels
in 1974 - 1975
(Amounts in thousands)

Budget Mechanism	1972		1973		1974		1975	
	No.	Amount	No.	Amount	No.	Amount	No.	Amount
Research Grants:								
Regular:								
Non-competing	719	$54,553	963	$59,544	918	$55,420	1,252	$72,720
Competing	207	13,960	154	14,259	136	13,538	98	8,884
New	292	14,354	173	8,830	269	12,248	113	5,780
Supplemental	(39)	1,019	(24)	523	(34)	870	(21)	546
Subtotal	1,218	83,886	1,290	83,156	1,323	82,076	1,463	87,930
Special:								
Pharm-Tox. Res. Centers	11	5,593	11	5,593	11	5,320	13	6,500
Anesth. & Diag. Rad. Centers	3	2,066	5	2,126	5	2,090	8	4,000
Genetic Res. Centers	5	3,000	8	3,000	10	5,985	13	7,000
Trauma Centers	--	---	--	---	8	1,900	15	5,000
Biomed. Eng. Centers	--	---	--	---	4	1,425	6	2,000
Molecular Pathology Centers	--	---	--	---	1	475	1	500
Research Career Program	377	8,648	354	8,280	296	7,740	233	6,277
Scientific Evaluation	--	377	--	372	--	348	--	366
Subtotal	396	19,684	378	19,371	335	25,283	289	31,643
Total Research Grants	1,614	103,570	1,668	102,527	1,658	107,359	1,752	119,573
Fellowships:								
Non-competing	446	2,655	360	2,515	243	2,429	812	11,107
Competing	19	172	13	134	3	35	20	260
New	414	4,131	147	1,531	469	7,300	321	4,931
Supplemental	(--)	---	(--)	49	(--)	50	(--)	50
Subtotal	879	6,958	520	4,229	715	9,814	1,153	16,348
Training Grants:								
Non-competing	395	37,628	352	24,540	376	34,507	530	33,090
Competing	65	5,760	91	8,275	1	93	--	---
New	3	238	3	165	5	503	--	---
Supplemental	(9)	120	(3)	20	(430)	13,952	(--)	---
Subtotal	463	43,746	446	33,000	382	49,055	530	33,090
Total Grants	2,956	154,274	2,634	139,756	2,755	166,228	3,435	169,011
Res. & Development Contracts	16	4,814	17	4,312	12	5,886	12	3,993
Res. Management & Program Services	--	5,644	--	5,904	--	6,993	--	6,901
TOTAL	2,972	164,732	2,651	149,972	2,767	179,107	3,447	179,905

Obligations by Budget Activity
Showing "True" Program Levels
in 1974 - 1975
(Amounts in thousands)

Budget Program	1973		1974		1975	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Pharmacology-Toxicology	--	$23,378	--	$27,902	--	$28,040
Biomedical Engineering	--	17,963	--	21,357	--	21,462
Clinical and Physiological Sciences	--	20,247	--	24,112	--	24,232
Genetics	--	40,175	--	47,880	--	48,118
Cellular and Molecular Basis of Disease	--	42,721	--	51,331	--	51,583
Research Management and Program	170	5,488	155	6,525	155	6,470
TOTAL	170	149,972	155	179,107	155	179,905

DISTRIBUTION OF 1973
IMPOUNDED FUNDS
(Dollars in thousands)

Budget Mechanism	No of Awards	Amount	Remarks
Research Grants	17	$704	Pharmacology-Toxicology
	19	803	Biomedical Engineering
	8	357	Clinical & Physiological Sciences
	51	1,963	Genetics
	41	1,597	Cellular & Molecular Basis of Disease
Fellowships	42	670	Pharmacology-Toxicology
	21	300	Biomedical Engineering
	14	200	Clinical & Physiological Sciences
	46	776	Genetics
	52	884	Cellular & Molecular Basis of Disease
Training Grants 1/	1	1,350	Pharmacology-Toxicology
	1	1,625	Biomedical Engineering
	3	4,252	Clinical & Physiological Sciences
	1	972	Genetics
	4	6,312	Cellular & Molecular Basis of Disease
Research & Development Contracts	1	405	Pharmacology-Toxicology
	1	367	Biomedical Engineering
	--	---	Clinical & Physiological Sciences
	1	300	Genetics
	--	---	Cellular & Molecular Basis of Disease
Research Management and Program Services	--	41	Research Management & Program Services
TOTAL	324	23,878	

1/ The impounded funds of $14,511,000 for training grants was used primarily for the restoration of 424 already existing training grants.

Multi-Year Funding from
1974 Appropriation

(Amounts in Thousands)

Budget Mechanisms	No. of Awards	Total Amount	Amount Affecting 1975 Funding	Remarks
Research Grants	16	$ 1,994	$ 997	Pharmacology-Toxicology
	16	1,874	937	Biomedical Engineering
	1	48	24	Clinical & Physiological Sciences
	43	5,212	2,606	Genetics
	24	2,882	1,441	Cellular & Molecular Basis of Disease
Fellowships	74	2,320	1,160	Pharmacology-Toxicology
	13	510	255	Biomedical Engineering
	3	56	28	Clinical & Physiological Sciences
	33	850	425	Genetics
	65	1,924	962	Cellular & Molecular Basis of Disease
Training Grants	10	740	370	Pharmacology-Toxicology
	7	494	247	Biomedical Engineering
	5	412	206	Clinical & Physiological Sciences
	23	1,700	850	Genetics
	29	2,136	1,068	Cellular & Molecular Basis of Disease
TOTAL	362	$23,152	$11,576	

NEW RESEARCH GRANTS

Mr. Flood. How many new research grants are you going to award or will you award in 1975?

Dr. von Euler. 211.

Mr. Flood. Is that the same as last year?

Dr. von Euler. Last year, that is to say this year the number is 383. I am adding now competing awards and new awards.

Mr. Flood. Is it the same level as last year?

Dr. von Euler. It is smaller.

ACUPUNCTURE

Mr. Flood. I notice you didn't say a word in your opening statement about acupuncture.

Dr. von Euler. That is right.

Mr. Flood. That has become sort of a sacred cow around here. Last year Dr. Stetten told us he thought your Institute would fund at least some research in that area. Are you, and if so, what is the extent of the effort?

Dr. von Euler. We have funded three grants in the area of acupuncture. We have had, NIH-wide, 30 applications; 5 of those have been funded, 3 by our Institute.

Mr. Flood. For the record you had better indicate where, when, who, how much, and so on. Have the record show this because there will be considerable interest in acupuncture. Tell us about it.

[The information follows:]

During the past year, the Institute, along with several others at NIH, has continued to explore the mode of action of acupuncture through the award of research grants, participation in conferences, and by bringing together information already in the literature or under development in laboratories throughout the country. There has been great interest in the published proceedings of the NIH Acupuncture Research Conference. Copies have been distributed widely and are available on request from NIH. Noteworthy is the growing interest at the State licensing board level. The small proportion of funded research grants reflects the fact that this is a new area of research in which few are qualified to work. Twenty of the 30 applications received were disapproved. We are working with these applicants, giving them the critique of the scientific reviewers, and helping them strengthen their programs. A list of grants and other currently funded NIH activities follows:

STATUS OF ACUPUNCTURE RESEARCH AT NIH—EXTRAMURAL RESEARCH

Principal investigator/institution	Title	Date awarded	Amount
Smith, G. M.: Massachusetts General Hospital, Boston, Mass.	Studies of acupuncture in dental pain.	April 1974	$78,934
Ulett, G. A.: Missouri Institute of Psychiatry, St. Louis, Mo.	Hypno- and acupuncture-analgesia physiological study.	January 1974	34,856
Perl, E. R.: University of North Carolina, Chapel Hill, N.C.	A controlled study of acupuncture and skin sensation.	January 1974	20,000
Sung, Y. F.: Emory University, Atlanta, Ga	Acupuncture anesthesia and analgesia.	February 1974	15,080
Sugioka, K.: University of North Carolina, Chapel Hill, N.C.	Evaluation of acupuncture in hypertension therapy.	January 1974	35,113

In addition, NIGMS Anesthesiology Centers in Seattle, San Francisco, and Boston are conducting studies on acupuncture.

INTRAMURAL RESEARCH

There are two intramural NIH research projects on acupuncture. One deals with the control of drug withdrawal symptoms in laboratory animals (NIMH), and the other deals with the physiological and psychological responses of human beings to acupuncture needling (NINDS).

ANESTHESIOLOGY CENTERS

Mr. Flood. Are any of your anesthesiology centers studying acupuncture?

Dr. von Euler. Yes, our center in Seattle, Wash., is studying it from several points of view, both from the pain and behavioral science point of view, and from an efficacy point of view in the pain clinic which is partially financed by NIGMS.

Mr. Flood. Is that the only one?

Dr. von Euler. It is most active. Two other centers have pilot studies underway.

Mr. Flood. I don't think the record shows the number and location of the anesthesiology centers. I don't think we have that.

Dr. von Euler. I can give it to you.

Mr. Flood. Place it in the record.

[The information follows:]

ANESTHESIOLOGY CENTERS

Principal investigator/institution	Fiscal year (total cost)— 1974	Fiscal year (total cost)— 1975
Ngai, Shih-Shun: Columbia University, New York, N.Y.	$338,897	$373,504
Wollman, Harry: University of Pennsylvania, Philadelphia, Pa	418,824	464,678
Hamilton, William K.: University of California, S.F., San Francisco, Calif	405,749	405,507
Kitz, Richard J.: Massachusetts General Hospital, Boston, Mass	625,671	565,401
Bonica, John J.: University of Washington, Seattle, Wash	507,203	598,167
Total	2,296,344	2,407,257

ANESTHESIOLOGY

Mr. Flood. In your justifications you state "Anesthesiology is considered one of the undermanned medical specialties and the shortage of research-trained medical faculty is particularly serious."

Who considers this an undermanned specialty? Who thought that up?

Dr. von Euler. This is on the basis of advice from consultants and conferences we have convened who have studied the manpower problem in anesthesiology.

Mr. Flood. Conferences with whom?

Dr. von Euler. Academic anesthesiologists serving on the NIGMS Anesthesiology Training Committee.

Mr. Flood. What is an academic anesthesiologist; somebody on the faculty someplace?

Dr. von Euler. Yes. At the medical schools.

Mr. Flood. Don't you have any source of information other than the faculties outside of the academic world, as to whether or not these are undermanned? Would anybody else have an opinion? What about hospital centers and the professions?

Dr. von Euler. A large number of the anesthetics in this country are given by nurse anesthetists. I believe at least 50 percent of anesthesia is administered in that fashion.

Mr. Flood. Do you mean paramedics?

Dr. von Euler. They are much better trained than that.

Mr. Flood. But there is somebody else there, I hope?

Dr. von Euler. Yes.

Mr. Flood. What are you doing in the 1975 budget to remedy the situation, if that is a fact? You conclude from your statement that this is true as a fact.

Dr. von Euler. That is right.

Mr. Flood. In your 1975 budget what are you doing about it?

Dr. von Euler. We are requesting money to support postdoctoral research fellowships in this area.

Mr. Flood. How many?

Dr. von Euler. The number hasn't been set absolutely. It depends on the quality of the applicants we get.

Mr. Flood. Do you have any applications in your pocket? What is the situation? Is anybody fighting to get in here?

Dr. von Euler. The receipt of these applications has just been concluded so I don't have a very accurate figure.

Mr. Flood. What is a ball park figure?

Dr. von Euler. Strictly a guess, twenty or thirty individuals.

Mr. Flood. Nationwide?

Dr. von Euler. Yes. This was the first call for such fellowships and conceivably there will be a greater application pressure next deadline, which is May 1.

TRAINING GRANTS AND FELLOWSHIPS

Mr. Flood. Now your 1975 budget calls for a reduction of $7 million in training grants and a $3.7 million increase in fellowships. Is this one of those shifts again from the predoctoral emphasis to the postdoctoral emphasis?

Dr. von Euler. I think it represents that, yes, sir.

Mr. Flood. It is, isn't it?

Dr. von Euler. Yes.

Mr. Flood. You know it is?

Dr. von Euler. Yes.

Mr. Flood. Will that shift in funding and that reduction of about $4 million mean fewer trained individuals in 1975? If it does, how many?

Dr. von Euler. Fewer individuals in training in 1975, and 3 or 4 years later that many more would be missing from academic medicine if these individuals were not able to find alternative sources of funding.

Mr. Flood. How many fewer?

Dr. von Euler. We will be funding about 600 fewer predoctoral students in 1975. Of course, that figure does not account for the increase in postdoctoral fellowships we will be supporting.

Mr. Flood. 600 fewer individuals will be trained?

Dr. von Euler. That is right.

TRAUMA CENTERS

Mr. Flood. Again in your general statement you gave an example of one of the trauma centers for the treatment of severe burns. Do these centers work with or are they part of the emergency medical systems being supported by the Health Services Administration?

Dr. von Euler. We are looking into how these two can relate, but the legislation is quite new and I don't know the full answer to your question.

Mr. Flood. As of now they are not working together?

Dr. von Euler. Not closely, that is right.

Mr. Flood. Then I will have to say, if they are not, why aren't they? What is your answer to that?

Dr. von Euler. If you are referring to the legislation I believe it was only passed 3 months ago.

Mr. Flood. What do you want—3 years?

Dr. von Euler. No, not necessarily.

Mr. Flood. Can't you tell me something about the 3 months? What are you waiting for?

Dr. von Euler. I assume there is local collaboration being set up at the eight centers we currently have.

Mr. Flood. Doesn't somebody know? These are your centers and here they are dealing with trauma, and this is the emergency medical system. Are you working with the emergency medical system program in the Health Services Administration?

Dr. Stetten. The centers which are supported by the General Medical Sciences Institute are centers for research. Clearly, they are physically associated with the emergency program in general major hospitals. This is where they get the material for the research they do.

On the other hand, the service aspect has, I think, systematically been minimized because that is not a recognized responsibility of this institute.

Mr. Flood. Is there a quarrel about jurisdiction now?

Dr. Stetten. No, there is no quarrel. That is just the point. Maybe there should be but there isn't.

Dr. von Euler. We are frequently in touch with the people at the HSA for information. We are aware of what they are doing in the field.

Mr. Flood. How many of these trauma centers will you have in operation by the end of fiscal 1975?

Dr. von Euler. We have eight now.

Mr. Flood. By the end of 1975?

Dr. von Euler. We expect to have 15.

Mr. Flood. Do we have a list of those, how they are distributed geographically?

Dr. von Euler. We have a list of the eight currently active, yes.

Mr. Flood. By the time this record is printed, you should have a better awareness of the 15 by the end of fiscal 1975, shouldn't you? People are going to ask us.

Dr. von Euler. If I may, it takes considerable time to program these, and until we have the money closer at hand, at least, programing efforts are somewhat inhibited but we proceed all the same.

Mr. Flood. What I mean is be sure you have in a thing like this proper geographical balance.

Dr. von Euler. May I ask are you saying that with regard to the research centers as well?

Mr. Flood. Yes.

[The information follows:]

Currently supported trauma research centers are located in Albany, Boston, Buffalo, Cincinnati, Dallas, Jackson, Miss., New York, and San Francisco. We have had numerous inquiries and are aware of plans to submit applications from institutions in Charlottesville, Los Angeles, Miami, St. Louis, and Seattle. All of these centers, existing as well as planned, are research centers in large, university-affiliated hospitals and have developed close ties and collaboration with local or Federal emergency medical services.

TRAUMA CENTERS

Principal investigator/institution	Fiscal year (total cost)—	
	1974	1975
Kinney, John M.: Columbia Presbyterian Medical Center, New York, N.Y.	$441,235	$494,253
Shires, George J.: University of Texas, Dallas, Dallas, Tex.	363,831	340,225
Powers, Samuel: Albany Medical Center, Albany, N.Y.	147,114	166,379
Altemeier, William: Cincinnati General Hospital, Cincinnati, Ohio	397,487	398,432
Schenk, Worthington G.: SUNY at Buffalo, Buffalo, N.Y.	171,209	194,216
Egdahl, Richard: Boston University, Boston, Mass.	196,818	216,520
Hardy, James D.: University of Mississippi, Jackson, Miss.	100,000	108,591
Blaisdell, William: San Francisco General Hospital, San Francisco, Calif.	154,854	296,844
Total	1,972,548	2,215,460

AUTOMATED LABORATORIES

Mr. Flood. On biomedical engineering, in your justifications you state that one goal of the biomedical engineering program is to develop "modular automated clinical laboratory systems that can benefit all sizes of hospitals."

Will any of these automated systems be suitable for the HMO's which are going to care for as many as 40,000 enrollees?

Dr. von Euler. They would be applicable both to small and to large hospital and laboratory operations.

Mr. Flood. You know why I ask you because the HMO bill was recently enacted, and we are going to have a lot of them all over the place in the next couple of years. So you have to keep that in mind.

Will these automated laboratories reduce the cost of the tests and save money for the man in the street?

Dr. von Euler. They will reduce the cost of some of the common familiar tests and will make the performance of many of these more accurate. But all along new tests are developed in the medical laboratories and some of the new ones, especially tend to be expensive. So considering the overall costs, I don't know that we can promise a decrease.

GENETIC COUNSELING

Mr. Flood. In your general statement you point out the need for some research in medical ethics with respect to genetic counseling, and you said you thought to conduct such a study you need the support of the Health Services Administration.

Dr. von Euler. That is correct.

Mr. Flood. Have they committed any of their resources to the study?

Dr. von Euler. They have not made a commitment. We approached them 2 months ago to see whether they had an interest, which they do have, and they will further help us to set up the conference later this year.

Mr. Flood. Suppose you tell us something about the study.

Dr. von Euler. The genetic counseling, as I mentioned, is going on in a scattered fashion in several centers and elsewhere in the country. We have had a number of applications for support of those studies, but in most cases the number of patients involved has been too small.

Furthermore, the studies have not been done in a uniform way so that they could be pooled with others in sufficient numbers. What we hope to do is set up the requirements for the study, and then elicit the collaboration and cooperation of as many centers as possible.

CELLULAR AND MOLECULAR BASIS OF DISEASE

Mr. Flood. Also in your statement you place considerable emphasis upon the importance of the cellular and molecular basis of disease program. But in your budget you propose a $2.9 million cut in this program. You make a big speech about the program, and then I turn the page and there is a $2.9 million cut. How do you reconcile the importance you place on the program with one hand and a cut with the other? We are getting kind of used to that, but I want your answer.

Dr. von Euler. A large portion of the budget for the current year represents support of predoctoral research training. Since that is falling off next year the large negative part of that is dominant. The research budget for this program is going up in terms of activity, considering some multiyear funding this fiscal year.

Mr. Flood. That kind of double talk at NIH is unusual, you see. There are other agencies, whose names I will not burden the record with at this point, who make a practice out of "for God, country, and Yale," and then bang, they cut it apart at OMB on Tuesday. I am wondering about that in your shop. You almost broke down and cried about this program, and then you cut it $2.9 million.

Dr. von Euler. As I said, I think the cut represents primarily a cut in training.

Mr. Flood. Mr. Patten.

PSORIASIS

Mr. Patten. You used the expression "psoriatic arthritis." Does it mean what I think it means? Are you associating psoriasis and arthritis?

Dr. von Euler. One form of arthritis is associated with psoriasis and is thought to be part of the disease process in some patients.

Mr. Patten. What is that new drug, what is its nature? I have 500,000 people in New Jersey working in the chemical industry.

Dr. von Euler. It is an analog which as a matter of fact was partially developed by a man in New Jersey at one of the drug companies. It is an analog of one of the components of nucleic acid genetic material. It is thought to interfere with the reproduction of the cells in the epithelium.

Mr. Patten. Do you have a little ray of hope you might have something?

Dr. von Euler. Yes, I think we do.

Mr. Patten. In your justification book your department is No. 1. I don't know why we are taking you up last. There is no point in that. You are No. 1 yet you are last. Do you think you are top man on the totem pole at NIH, General Medical Sciences?

Dr. Stetten. We have a great fondness for our Institute.

Mr. Patten. Do you think the public generally associates NIH really with your department more than some of the others? You don't want to answer that. You are too modest. I will say I think so on the public impression of what you are supposed to do. You have a great department.

You probably didn't hear me say, Dr. von Euler, when people complain about our Government, the Post Office, Internal Revenue, and other departments I always say if they want to see how beautiful the Government is, go and visit NIH and find out what they are doing and you will be proud of the United States. You work hard so we will be able to make that true statement. Because I do believe the most beautiful part of the Federal Government is in HEW. NIH is the hope of many Americans and I wish you the best of success in your work.

I have no further questions.

Mr. Flood. Mr. Obey.

TRAINING PROGRAMS

Mr. Obey. In the past evidently your Institute has had the primary responsibility within NIH of support of predoctoral research training. The chairman has asked you some questions about the training situation. In your personal judgment is the research training program now being operated as suggested in this budget adequate both in terms of the number of individuals to be trained and the type of training to be given to meet the needs of future NIH-sponsored research efforts?

Dr. von Euler. There are two parts to the training endeavors in our Institute. I believe that the new fellowship programs in the postdoctoral field will adequately take the place of efforts in the past.

With regard to the support for predoctoral training, this is now being shifted over to be funded on the basis of loans, and whether that will be equally effective I just don't know, at this point in time.

Mr. Obey. There is a large measure of room for doubt, isn't there?

Dr. von Euler. It has not been tested in a long time. Originally 30 or 40 years ago there wasn't this kind of support for predoctoral training.

PHARMACOLOGY TRAINING

Mr. Obey. I have been told there is a need for more broadly trained pharmacologists to apply new knowledge to large scale application of patient care. Given the situation with physician treatment, what is the current situation and what is the future picture for your Institute program of training pharmacologists at NIH?

Dr. von Euler. The only intramural activity our Institute is involved in is the support of 18 research associates at the clinical center of NIH.

There was earlier a larger number of them, but right now I would say the number is somewhat limited by——

Mr. Obey. You say there was a larger number earlier?

Dr. von Euler. Several years ago.

Mr. Obey. Take 2 or 3 years ago. What were the numbers?

Mr. Klovdahl. We had 30 in the budget.

Mr. Obey. Two years ago 30?

Mr. Klovdahl. Earlier than that. I believe in 1969.

Mr. Obey. Now you are down to 18?

Dr. von Euler. That is right.

Mr. Obey. What is your projection for the next 2 or 3 years?

Dr. von Euler. We are projecting the same number of 18 for 1975, and I assume the same for the years after that.

Mr. Obey. Do you think a decent case could be made for more?

Dr. von Euler. Yes; I do.

Mr. Obey. That is all the questions I have. Thank you.

GENETICS

Mr. Casey. Your genetic research is relatively new is it not? I mean the emphasis on it?

Dr. von Euler. That is correct.

Mr. Casey. Not that you weren't doing some before, but I think the committee urged your emphasis on it, and you are now placing more emphasis on genetic research.

What do you propose to spend in genetic research in the proposed budget?

Dr. von Euler. Next year we expect to spend a total of $46 million in our genetic program including expenditures for research and training.

Mr. Casey. How does that compare with last year?

Dr. von Euler. Compared to the budget excluding the impounded money, it is a little less than a $1 million increase.

Mr. Casey. $1 million less?

Dr. von Euler. It is just under $1 million more—$900,000 more.

Mr. Casey. What was in the appropriation last year? You say this is $1 million more than the funds released. Is that correct?

Dr. von Euler. It is $1 million more than our 1974 budget before the release of 1973 funds.

Mr. Casey. In other words, it is about the same level?

Dr. von Euler. That is correct. The release added $4 million.

Mr. Casey. I notice in your statement that you seem to be pleased with the way the research is progressing.

Dr. von Euler. Yes, sir.

Mr. Casey. It is opening a whole new horizon in various fields such as cancer?

Dr. von Euler. It does feed into a number of other areas.

Mr. Casey. Cystic fibrosis?

Dr. von Euler. That is right and heart disease.

Mr. Casey. I want to commend you on following the committee's recommendation. I hope you continue, because from what I have learned I think it is a horizon that needs to be further explored and we need to put as much emphasis on it as we can, considering your other obligations and commitments. I think it offers a lot for us in the future. Thank you, Mr. Chairman.

TRAINING PROGRAM

Mr. Conte. Is it true that NIGMS has, in the past, supported the largest amount of predoctoral training of all the NIH Institutes?

Dr. von Euler. Yes, sir.

Mr. Conte. If the emphasis on training support at the postdoctoral level persists, are you going to have enough good students getting through the Ph. D. or M.D. to meet your needs in basic research?

Dr. von Euler. NIGMS supports predoctoral research training in the basic biomedical sciences at highly selected institutions and departments, the selection being based on the quality of graduate and research training as judged by peer review groups. Consequently, insofar as possible, only the best part of the graduate student body in these fields has been selected for support, the rest having had to finance their studies through loans, part-time jobs, and so forth. If NIH predoctoral support is eliminated, potential trainees may find other means of supporting their studies, but the proportion is unknown. Also unknown is the effect of the elimination of predoctoral support on the quality of graduate and research training.

Mr. Conte. Do you have any projections of the number of students in the basic medical sciences who can be expected to get past the doctorate level without the kind of support they've had in the past?

Dr. von Euler. We do not have reliable projections on this point. I would guess that one-half of the currently supported individuals would have gone through this training by other financial means. We are particularly concerned with the unusually gifted students who may lack the means to obtain such training.

Mr. Conte. In research, you seem to be going more and more in the direction of institutional support, that is, support of a few large centers. In research training, you're going exactly the opposite way—support of individuals only. How do you reconcile these two policies?

Dr. von Euler. We support large centers in order to bring together scientists and research projects from several disciplines, and to facilitate the translation of laboratory research findings to the clinic. While the centers include institutional support for the core facilities, the greater proportion of funds is earmarked for specific projects. By virtue of their sheer size, centers can have great impact on institutions, and their initiation or abrupt termination may unduly disrupt the overall function of a medical school. We would, therefore, like to see the size of individual centers, as well as the proportion of our total budget spent on centers, limited and kept under control. The old research training grants were generally much smaller than the average center, but included a variable proportion, averaging about 50 percent, for partial funding of salaries for faculty and supporting staff, equipment, and other institutional costs essential to the research training function. While the institutional fellowship programs announced last year by Secretary Weinberger allow a portion of the total award for institutional support, the major support of research training will now be, as you state, through individual postdoctoral fellowships.

RESEARCH GRANTS

Mr. Conte. In every field you cover, you will have substantial reductions for new research grants in 1975. What does this mean for the young researcher? Or for the researcher with an offbeat idea?

Dr. von Euler. Any reduction in funds for new grants may hit the young and still unknown investigator harder than the established scientist, despite our conscious efforts to protect him or her. The same can be said for the researcher with an offbeat idea. Appreciation and acceptance of new and unusual scientific proposals is a challenge to the peer review system and is under close scrutiny at NIH currently.

Mr. Conte. Will you provide for the record the priority level at which you cut off making new awards for approved research projects in 1972 and 1973, and will you estimate that for 1974 and 1975?

[The information follows:]

[Fiscal years]

	1972	1973	Estimate 1974	Estimate 1975
Type 1 (new)	230	208	185	165
Type 2 (competing renewals)	235	200	205	185

CELLULAR PATHOLOGY

Mr. Conte. Do you have any more centers in cellular pathology in the planning stage?

Dr. von Euler. Following last year's congressional authorization of Molecular Pathology Centers, we formally announced to the scientific community that we would accept applications for such centers. In response, we have received many inquiries. In discussions with these institutions, it is apparent that at least 10 are in the planning stage and will be submitting applications soon.

BURNS

Mr. Robinson. On page 2 you mention that the immunological matching of cadaver skin under hypotensive anesthesia has been highly successful in treating severe burn cases. How difficult is the matching process involved? How many types of skin are there that must be matched?

Dr. von Euler. The matching process used by our grantees was based only on the common ABO blood types. While this appears to have been enough in a number of cases, failures in having transplants take have been numerous enough to show the need for refinement. Attempts to use tissue-typing in the way it has been used for kidney transplantation have generally failed. A workable method to type and match cadaver skins is therefore thought to be an important area of future investigation. How many types of skin would need to be distinguished in this manner is not known.

PSORIASIS

Mr. Robinson. On page 3 you mention that a drug known as azaribine has been found to be very effective in cases of severe psoriasis and that this disease may result in death. How many cases of death resulting from psoriasis have been recorded in the last 3 years on an annual basis? What is the FDA status on the drug azaribine? Is it being tested for release by that agency?

Dr. von Euler. The annual death rate from psoriasis proper ranged from 13 to 19 during the last 3 years for which we have data; namely, 1968–70. There are reasons to believe these figures are low. The clinical research center in Providence, R.I., has about two deaths a year which can be attributed to psoriasis, but as a center with a special interest in the disease, it may attract unusually large numbers of these patients. Serious morbidity is an important problem, occasionally leading to suicide. In spite of its importance, we could not find good data on hospitalization for psoriasis, except for the VA system of hospitals, which discharged 1,093 such patients in 1968. Azaribine is classified by FDA as an investigational drug, used only under "investigational new drug" exemption. When or if satisfactory documentation of its safety and efficacy has been accumulated, it may be released for general use.

CELL REPOSITORY

Mr. Robinson. On page 4 you mention the operation of a repository for a variety of human cell types and small pieces of tissue from individuals suffering from different genetic diseases. From what genetic diseases are the victims suffering from whom these small pieces of tissue are collected?

Dr. von Euler. The Mammalian Mutant Cell Repository collects tissues and grows and distributes cells from patients suffering from a variety of genetic diseases. For comparison, cells from unaffected relatives are also collected.

Examples of diseases that are represented in the collection can be supplied for the record.

[The information follows:]

Metabolic diseases:
  Citrullinuria.
  Cystinosis.
  Galactosemia.
  Glycogen storage diseases.
  Huntington's Chorea.
  Hurler and Hunter syndromes.
  Lesch-Nyhan syndrome.
  Phenylketonuria.
  Tay-Sachs disease.

Chromosomal abnormalities: Translocations and trisomies that are expressed in such conditions as Down's syndrome—mongolism—Klinefelter's syndrome. and the Cri du Chat syndrome.

GENETIC BLOOD TESTS

Mr. Robinson. Regarding the perfecting of a simple blood test to test the genetic differences with respect to the reaction to smoking, how long do you estimate that it will be before such a test will be generally available for use?

Dr. von Euler. Regarding the question of blood tests for a genetic predisposition toward lung cancer, especially among smokers, the grantee, Dr. Charles R. Shaw, University of Texas, informs us that there are six to eight research centers in the country that currently use the test for research purposes. All have visited Dr. Shaw's laboratory, and have ironed out differences in technique or protocol.

Dr. Shaw estimates that at these centers, the test is likely to be available for diagnosis in 6 months to a year. Costs run high; around $24 per test for materials; total cost, including labor, may be around $50.

The diffusion of this test into the general hospital clinical laboratory would be slower and may take some years.

GENETICS COUNSELING

Mr. Robinson. You mention that experience with a greater number of patients is necessary before genetic counseling can be statistically valid. How many patients would constitute a sufficiently large sample in order to be statistically valid?

Dr. von Euler. Although some genetics clinics see hundreds of patients per year, it would be desirable, in assessing the effect of genetic counseling, to choose subgroups that are reasonably homogeneous; for example, older mothers at risk for Down's syndrome. This would generally make the numbers at any one center fairly small, and in the judgment of our advisors, insufficient to permit valid conclusions. How many patients would be required for a valid study we do not yet know.

Other reasons for extending the scope of the study, not stressed in the necessarily short presentation, relate to differences in research emphasis among the genetics centers, and the fact that genetic counselors are usually not well versed in the methods of social research. To do the work at one center would mean that one or a few counselors would, in effect, evaluate their own performance. It seems more reasonable to devise a common protocol for several centers, which could be followed uniformly. The study would first have to ask: What different measures of "effectiveness" should be considered?

Mr. Robinson. How soon will the fact sheet entitled "What are the Facts About Genetic Disease, Most Ubiquitous of All Human Maladies?" be available?

Dr. von Euler. It is available now, in draft form, from the National Institute of General Medical Sciences. We will send final copies to the subcommittee members as soon as they are received from the printer.

MITOCHONDRIAL DISEASES

Mr. Robinson. You seem to zero in on the subject of mitochrondrial diseases in a very significant way. How much of your total research budget is devoted to this area?

Dr. von Euler. About $2.9 million. A number of diseases associated with mitochondrial abnormalities, such as thyrotoxicosis, obesity, and alcoholism, are the responsibility of other Institutes. The NIGMS responsibility with regard to these diseases has been the steady refinement of our understanding of them at the subcellular level. Our grantees are discovering basic characteristics and details about the structure and function of mitochondria. To speed the translation of this knowledge into better diagnosis and treatment, NIGMS is supporting the development of molecular pathology centers where, for instance, cell biologists can study mitochondria and their role in disease alongside pathologists and clinical investigators.

BIOMEDICAL ENGINEERING

Mr. Robinson. With respect to biomedical engineering, my impression is that there is a substantial effort in this area at the medical center of the University of Virginia. Are you aware of this, and, if so, do you support any part of this effort?

Dr. von Euler. We are well acquainted with the biomedical engineering effort at the University of Virginia. Ernst O. Attinger—a physician and engineer, and chairman of the division of biomedical engineering at the University of Virginia—has served as chairman of the Institute's biomedical engineering training committee. In this capacity he was a major contributor to the Institute's report on "The Future of Training in Biomedical Engineering."

Presently he is the director of a predoctoral research training program in biomedical engineering at the University of Virginia that is supported by us at a level of $100,059. A highlight of this program is the degree of interaction that exists between the school of engineering and the school of medicine.

A portion of the Institute's biomedical engineering program is concerned with the automation of clinical laboratories. At the University of Virginia we currently support three research projects in this area.

Mr. Flood. Thank you very much.

JUSTIFICATION OF THE BUDGET ESTIMATES

NATIONAL INSTITUTES OF HEALTH

National Institute of General Medical Sciences

Amounts Available for Obligation

	1974 Revised	1975
Appropriation	$176,778,000	$168,329,000
Amount withheld (PL 93-192)	-8,449,000	---
Subtotal, adjusted appropriation	168,329,000	168,329,000
Comparative transfer to:		
"Office of Assistant Secretary for Health" (Transfer of administrative support activities to the Office of the Assistant Secretary for Health)	-44,000	---
"National Cancer Institute"	-279,000	---
"National Heart and Lung Institute"	-358,000	---
"National Institute of Dental Research"	-36,000	---
"National Institute of Arthritis, Metabolism, and Digestive Diseases"	-256,000	---
"National Institute of Neurological Diseases and Stroke"	-152,000	---
"National Institute of Allergy and Infectious Diseases"	-150,000	---
"National Institute of Child Health and Human Development	-155,000	---
"National Eye Institute"	-60,000	---
"National Institute of Environmental Health Sciences"	-24,000	---
"National Library of Medicine" (Decentralization of scientific evaluation grants program)	-10,000	---
Subtotal, budget authority (base obligations)	166,805,000	168,329,000
Unobligated balance, restored	29,177,000	---
Comparative transfer of restored unobligated balance to Research Resources for General Research Support Grants	-5,299,000	---
Total, obligations	190,683,000	168,329,000

Summary of Changes

1974 Estimated obligations	$190,683,000
1975 Estimated obligations	168,329,000
Net change	-22,354,000

	1974		Change from 1974	
	Pos.	Amount	Pos.	Amount
Increases:				
A. Built-in:				
1. Within-grade pay increase cost	---	---	---	+$30,000
2. Extra day of pay in F.Y. 1975	---	---	---	+11,000
3. FTS rate increase	---	---	---	+20,000
4. Bureau of Employment Compensation rate increase	---	---	---	+1,000
5. RMPS - Annualization cost of October 1973 pay raise	---	---	---	+36,000
6. Pharmacology-toxicology - Annualization cost of October 1973 pay raise	---	---	---	+4,000
Subtotal	---	---	---	+102,000
B. Program:				
1. Research Grants				
a. Noncompeting continuations	---	$55,420,000	---	+11,295,000
2. Special programs	---	14,555,000	---	+8,686,000
3. Fellowships				
a. Noncompeting	---	2,429,000	---	+5,848,000
Subtotal	---	---	---	+25,829,000
Total, increases	---	---	---	+25,931,000
Decreases:				
A. Built-in:				
1. Annualization of savings from employment reduction in 1974	---	---	---	-75,000
2. Payment to "NIH Management Fund" for centrally furnished services	---	---	---	-119,000
Subtotal	---	---	---	-194,000
B. Program:				
1. Competing continuations, regular research grants	---	32,661,000	---	-17,451,000
2. Special programs	---	10,253,000	---	-2,326,000
3. Fellowships				
a. Competing	---	10,215,000	---	-4,974,000
4. Training grants	---	51,796,000	---	-21,447,000
5. Research & Development Contracts	---	5,886,000	---	-1,893,000
Subtotal	---	---	---	-48,091,000
Total, decreases	---	---	---	-48,285,000
Total, net change	---	---	---	-22,354,000

Explanation of Changes

Increases:

A. Built-in:

1. The total built-in increase of $102,000 will provide: $30,000 for within-grade pay increases in 1975; $11,000 for an extra day's pay in 1975; $20,000 for increased costs of using the Federal Telecommunications System; $1,000 for Bureau of Employment Compensation rate increase; $36,000 for the Research Management and Program Services portion of the October 1973 pay raise annualization cost; and $4,000 for the Pharmacology-Toxicology direct training program portion of the October 1973 pay raise annualization cost.

B. Program:

1. The total program increase of $25,829,000 will provide: $11,295,000 for noncompeting continuations, regular research grants; $8,686,000 for Special Programs, of which $1,416,000 is for Pharmacology-Toxicology Research Centers; $2,062,000 is for Anesthesiology and Diagnostic Radiology Centers: $1,015,000 is for Genetic Research Centers; $3,100,000 is for Trauma Centers; $575,000 is for Biomedical Engineering Centers; $500,000 is for Molecular Pathology Centers; $18,000 is for Scientific Evaluation Grants; and $5,848,000 is for noncompeting fellowships.

Decreases:

A. Built-in:

1. The total built-in decrease of $194,000 includes a decrease of $75,000 in annualized savings related to the 1974 employment reduction and a decrease of $119,000 in the payment to the NIH Management Fund for centrally furnished services such as patient care, receipt and initial review of all grant applications, computer services, maintenance of buildings and grounds, custodial services, communications, and transportation.

B. Program:

1. The total program decrease of $48,091,000 includes: $17,451,000 for competing projects, regular research grants; $2,326,000 for Special Programs, of which $236,000 is for Pharmacology-Toxicology Research Centers, $152,000 is for Anesthesiology and Diagnostic Radiology Centers, $475,000 is for Molecular Pathology Centers, and $1,463,000 is for Research Career Programs: $4,974,000 is for competing fellowships; $21,447,000 is for training grants; and $1,893,000 is for Research and Development Contracts.

Obligations by Activity

Page Ref.		1974 Base *		1975 Estimate		Increase or Decrease	
		Pos.	Amount	Pos.	Amount	Pos.	Amount
16	Pharmacology-Toxicology........	---	$24,654,000 (27,783,000)	---	$26,175,000	---	+$1,521,000 A
19	Biomedical Engineering.......	---	21,470,000 (24,565,000)	---	21,421,000	---	-49,000 B
21	Clinical and Physiological Sciences..	---	21,138,000 (25,947,000)	---	23,251,000	---	+2,113,000 C
24	Genetics...........	---	45,194,000 (49,205,000)	---	46,087,000	---	+893,000 D
26	Cellular and Molecular Basis of Disease..........	---	47,824,000 (56,617,000)	---	44,925,000	---	-2,899,000 E
28	Research Management and Program Services..........	155	6,525,000 (6,566,000)	155	6,470,000	---	-55,000 F
Total obligations (base).		155	166,805,000	155	168,329,000	---	+1,524,000
Total obligations........			(190,683,000)				

Explanation of Changes (by activity)

A) Pharmacology-Toxicology--The net increase provides for two or three additional Pharmacology-Toxicology Centers and 93 fellowship awards in clinical pharmacology and toxicology. A small built-in increase of $4,000 is included for the direct training program.

B) Biomedical Engineering--The net decrease reflects an increase in already existing Diagnostic Radiology Centers, one or two new Biomedical Engineering Centers, and fellowships, offset by decreases in regular research grants, research career awards, scientific evaluation, training, and contracts.

C) Clinical and Physiological Sciences--The net increase provides for two or three additional Anesthesiology Centers and six or seven Trauma Centers.

D) Genetics--The net increase reflects an increase in Genetic Research Centers, scientific evaluation, and fellowships, offset by a decrease in regular research grants, research career awards, contracts, and training grants.

E) Cellular and Molecular Basis of Disease--The net decrease reflects an increase of Molecular Pathology Centers, scientific evaluation, and fellowships, offset by decreases in regular research grants, research career awards, and training grants.

F) Research Management and Program Services--The net decrease reflects built-in increases of $139,000 offset by a built-in decrease of $75,000 and a decrease of $119,000 to the NIH Management Fund.

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* 1974 Base - Excludes 1973 appropriation restorations. Total obligations shown in parentheses.

Obligations by Object

	1974 Estimate	1975 Estimate	Increase or Decrease
Total number of permanent positions..................	155	155	---
Full-time equivalent of all other positions.............	5	5	---
Average number of all employees..................	160	160	---

	1974 Estimate	1975 Estimate	Increase or Decrease
Personnel compensation:			
Permanent positions..........	$2,666,000	$2,669,000	+$3,000
Positions other than permanent	81,000	81,000	---
Other personnel compensation..	49,000	49,000	---
Subtotal, personnel compensation.............	2,796,000	2,799,000	+3,000
Personnel benefits.............	304,000	306,000	+2,000
Travel and transportation of persons......................	163,000	163,000	---
Transportation of things........	34,000	34,000	---
Rent, communications, and utilities....................	275,000	295,000	+20,000
Printing and reproduction.......	140,000	140,000	---
Other services:			
Project contracts............	5,886,000	3,993,000	-1,893,000
Payment to NIH Management Fund	2,129,000	2,010,000	-119,000
Other........................	1,030,000	1,031,000	+1,000
Supplies and materials..........	68,000	69,000	+1,000
Equipment......................	54,000	54,000	---
Grants, subsidies, and contributions................	177,804,000	157,435,000	-20,369,000
Total obligations by object.	190,683,000	168,329,000	-22,354,000
Total obligations excluding 1973 appropriation restorations.............	166,805,000		

Significant Items in House and Senate Appropriations Committee Reports

Item	Action taken or to be taken
1974 House Report	
Genetics	
1. The Committee expects that the increase for research grants, training grants and fellowships provided by this bill will, in part, be used to establish additional genetic centers and to launch a training program for medical geneticists (page 38).	1. Applications for two additional genetic centers have been received and we expect to fund these in 1974. Available information indicates that numerous applications have been received for training in medical genetics.
Trauma	
1. Some of the additional funds should also be used to increase the number of trauma centers on accidental injury (page 38).	1. Increased emphasis is being given to the development of additional trauma centers. Several applications have been received and will be reviewed later this year.
1974 Senate Report	
Cellular and Molecular Basis of Disease	
1. The Committee is encouraged by the progress being made in the Cellular and Molecular Basis of Disease Program. The Committee believes that a significant portion of the Congressional increase should be devoted to this program including the initiation of the molecular pathology centers (pages 52-53).	1. We expect to receive applications for four pathology centers in 1974 and it is likely that at least one of these will be funded.
Biomedical Engineering	
1. The Committee believes there is greater need for interaction between engineers and biomedical scientists . . . that a portion of the Congressional increase should be used for the establishment of bioengineering centers which would . . . generate new and improved instruments and devices for the detection, diagnosis, and treatment of disease as well as study the fundamentals of the chiropractic profession . . . (page 53).	1. One biomedical engineering center was established this year and we expect a number of other institutions will submit applications in F.Y. 1974 and 1975. We are cooperating with the NINDS and HSA in studying what should be initiated in the chiropractic profession.

Significant Items (continued)

Automated Clinical Laboratories

1. The Committee also believes that the Institute should devote increased resources to the support of the automated clinical laboratories (page 53).	1. Increased emphasis is being given to the field of research.

Acupuncture

1. . . . the Committee recommends that the NIH study further the uses of acupuncture in regard to surgical analgesia, chronic pain and its effects upon patients. Further, an intense effort should be mounted to inform professional and lay people alike as to the feasibility and practicality of using acupuncture (page 36).	1. During the past year, the NIH Acupuncture Study completed several significant steps in its program to evaluate and to understand acupuncture. Research projects at medical schools (University of Missouri and University of North Carolina) have received grant support and are studying the effectiveness of acupuncture in relieving chronic pain and for controlling high blood pressure. Two intramural research programs have also been initiated on acupuncture treatment of drug withdrawal symptoms and chronic pain. In addition, the proceedings of the first NIH Acupuncture Research Conference have been published and widely distributed to professional societies, state medical licensing boards, appropriate Federal agencies, and interested individuals. The proceedings contain over 40 reports of acupuncture research findings in various medical and scientific problem areas, and probably represent the first collection of observations, theories, and debate available from American scientists and physicians.

Authorizing Legislation

Legislation	1975 Authorized	 Appropriation requested
Public Health Service Act Section 301--Grants programs.......	Indefinite	
Title IV, Part E, Institutes of Child Health and Human Development and of General Medical Sciences....	Indefinite	$168,329,000

National Institute of General Medical Sciences

Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
1966	$119,342,000	$119,342,000	$123,428,000	$121,909,000
1967	130,891,000	136,172,000	138,672,000	138,672,000
1968	152,051,000	152,051,000	154,540,000	152,027,000
1969	157,650,000	153,123,000	158,123,000	155,386,500
1970	146,161,000	146,161,000	166,171,000	156,517,000
1971	142,328,000	158,112,000	163,112,000	158,112,000
1972	143,873,000	161,364,000	171,364,000	166,387,000
1973*	167,217,000	173,765,000	196,594,000	173,965,000 *
1974	137,049,000	174,254,000	181,976,000	175,254,000 **
1975	168,329,000			

appropriation authority was the continuing resolution.
ation amount was the House Allowance, which was the
e House or Senate amounts in the first vetoed bill.

tion after reduction, $166,805,000.

Justification

National Institute of General Medical Sciences

Authorizing Legislation: Public Health Service Act, Title IV, Part E

	1974 Base *		1975 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits..........	155	$3,100,000	155	$3,105,000	---	+$5,000
Other expenses..........	---	163,705,000	---	165,224,000	---	+1,519,000
Total...........	155	166,805,000	155	168,329,000	---	+1,524,000

General Statement

The National Institute of General Medical Sciences supports a wide spectrum of basic and clinical biomedical research that seeks to provide an understanding of life processes that when altered or disturbed may lead to disease. This research relates to knowledge concerning the structural elements comprising living organisms, the diverse functions of various life processes and the development of implements for diagnosis and treatment of human disorders. Programmed research objectives are to elucidate the genetic, molecular, and cellular bases for diseases, to enable the safer and more effective use of drugs, to discover better ways for treatment of accident victims, and through the application of engineering approaches and manpower, to develop more rational automated laboratory procedures and techniques for use in health care delivery. The National Institute of General Medical Sciences also has principal responsibility for supporting, through training grants, young medical research scientists in a number of basic science disciplines. This support is provided in scientific areas closely related to several clinical disciplines through postdoctoral individual fellowship awards. In addition, special support is given to increase access of blacks and members of other racial or minority groups to careers in biomedical research and academic medicine through the minority access to research careers (MARC) training program.

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* Excludes 1973 appropriation restorations.

DHEW - National Institutes of Health

CROSSWALK - 1974 COLUMN 1975 PRESIDENT'S BUDGET

INSTITUTE: National Institute of General Medical Sciences
(In thousands of dollars)

Mechanism / Program	Research Grants								
	Regular Program		Specials						
	Non-competing	Competing	Multi-disciplinary Centers	Other	Training Programs Grants	Training Programs Fellowships	Research and Development Contracts	Other Direct Operations	Total
1974 Base Obligations									
1. Pharmacology-Toxicology.....	$7,588	$2,616	$5,320	$981	$3.467	$1,755	$2,500	$427	$24,654
2. Biomedical Engineering......	9,303	2,561	2,316	520	4,176	1,094	1,500	---	21,470
3. Clinical & Physiological Sciences..................	1,673	3,305	3,099	330	10,925	1,806	---	---	21,138
4. Genetics....................	19,818	11,044	5,985	2,892	2,498	2,143	814	---	45,194
5. Cellular & Molecular Basis of Disease................	17,038	8,016	475	3,060	16,219	3,016	---	---	47,824
6. Research Management & Program Services..........	---	---	---	---	---	---	---	6,525	6,525
(Management Fund).......								(2,129)	(2,129)
Subtotal...................	55,420	27,542	17,195	7,783	37,285	9,814	4,814	6,952	166,805
Unobligated Balance Restored									
1. Pharmacology-Toxicology.....	---	630	---	74	1,350	670	405	---	3,129
2. Biomedical Engineering......	---	732	---	71	1,625	300	367	---	3,095
3. Clinical & Physiological Sciences..................	---	307	---	50	4,252	200	---	---	4,809
4. Genetics....................	---	1,904	---	59	972	776	300	---	4,011
5. Cellular & Molecular Basis of Disease................	---	1,546	---	51	6,312	884	---	---	8,793
6. Research Management & Program Services..........	---	---	---	---	---	---	---	41	41
(Management Fund).......								(---)	(---)
Subtotal...................	---	5,119	---	305	14,511	2,830	1,072	41	23,878
Total Obligations..............	55,420	32,661	17,195	8,088	51,796	12,644	5,886	6,993	190,683

DHEW - National Institutes of Health

CROSSWALK - 1975 COLUMN 1975 PRESIDENT'S BUDGET

INSTITUTE: National Institute of General Medical Sciences
(In thousands of dollars)

Mechanism / Program	Research Grants								
	Regular Program		Specials		Training Programs		Research and Development Contracts	Other Direct Operations	Total
	Non-competing	Competing	Multi-disciplinary Centers	Other	Grants	Fellowships			
1. Pharmacology-Toxicology....	$8,604	$1,445	$6,500	$865	$2,822	$3,232	$2,276	$431	$26
2. Biomedical Engineering.....	10,268	1,415	2,972	494	3,399	1,595	1,278	---	2
3. Clinical & Physiological Sciences................	3,077	1,825	8,028	348	8,892	1,081	---	---	
4. Genetics..................	24,519	6,099	7,000	2,415	2,033	3,582	439	---	
5. Cellular & Molecular Basis of Disease..............	20,247	4,426	500	2,521	13,203	4,028	---	---	
6. Research Management and Program Services.........	---	---	---	---	---	---	---	6,470	
(Management Fund)......								(2,010)	
Total obligations..........	66,715	15,210	25,000	6,643	30,349	13,518	3,993	6,901	

National Institute of General Medical Sciences

Budget Mechanism

	1974*		1975	
	Number	Amount	Number	Amount
Research Grants:				
Regular:				
Non-competing	918	$55,420,000	1,152	$66,715,000
Competing	178	16,270,000	98	8,884,000
New	205	10,466,000	113	5,780,000
Supplemental	(31)	806,000	(21)	546,000
Subtotal	1,301	82,962,000	1,363	81,925,000
Special:				
Pharmacology-Toxicology Research Centers	11	5,320,000	13	6,500,000
Anesthesiology & Diagnostic Radiology Centers	5	2,090,000	8	4,000,000
Genetic Research Centers	10	5,985,000	13	7,000,000
Trauma Centers	8	1,900,000	15	5,000,000
Biomedical Engineering Centers	4	1,425,000	6	2,000,000
Molecular Pathology Centers	1	475,000	1	500,000
Research Career Programs	282	7,470,000	233	6,277,000
Scientific Evaluation	---	313,000	---	366,000
Subtotal	321	24,978,000	289	31,643,000
Total Research Grants	1,622	107,940,000	1,652	113,568,000
Fellowships:				
Non-competing	243	2,429,000	624	8,277,000
Competing	3	35,000	20	260,000
New	482	7,300,000	321	4,931,000
Supplemental	(---)	50,000	(---)	50,000
Subtotal	728	9,814,000	965	13,518,000
Training Grants:				
Non-competing	446	36,898,000	456	29,999,000
Competing	---	---	---	---
New	---	---	---	---
Supplemental	(6)	37,000	(---)	---
Scientific Evaluation	(2)	350,000	(2)	350,000
Subtotal	446	37,285,000	456	30,349,000
Total, Grants	2,796	155,039,000	3,073	157,435,000
Research & Development Contracts	12	4,814,000	12	3,993,000
Research Management and Program Services	---	6,952,000	---	6,901,000
TOTAL	2,808	166,805,000	3,085	168,329,000

* Excludes 1973 appropriation restorations.

Pharmacology-Toxicology

Authorizing Legislation: Public Health Service Act, Title IV, Part E

	1974 Base *		1975 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits...........	---	---	---	---	---	---
Other expenses...........	---	$24,654,000	---	$26,175,000	---	+$1,521,000
Total..........	---	24,654,000	---	26,175,000	---	+1,521,000

Budget Mechanism:

	1974 Base *		1975 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Research Grants:						
Regular program......	---	$10,204,000	---	$10,049,000	---	-$155,000
Special programs:						
Pharmacology-Toxicology Centers.....	---	5,320,000	---	6,500,000	---	+1,180,000
Research Career......	---	914,000	---	803,000	---	-111,000
Scientific Evaluation	---	67,000	---	62,000	---	-5,000
Subtotal Special...	---	6,301,000	---	7,365,000	---	+1,064,000
Fellowships............	---	1,755,000	---	3,232,000	---	+1,477,000
Training Grants........	---	3,467,000	---	2,822,000	---	-645,000
Research & Development Contracts...........	---	2,500,000	---	2,276,000	---	-224,000
Research Management & Program Services.....	---	427,000	---	431,000	---	+4,000
Total..........	---	24,654,000	---	26,175,000	---	+1,521,000

Plans in F.Y. 1975

The ongoing program of research grants, pharmacology-toxicology centers, training grants, fellowships, direct training, and research and development contracts will be pursued vigorously, with increases or special emphasis in the following areas: under the recent Institute reorganization, biorelated chemistry has been incorporated into the Pharmacology-Toxicology Program. Research in this area will be emphasized as well as in the areas of dermatopharmacology (skin), pharmacogenetics (the effect of genetic factors on an organism's response to drugs), pharmacokinetics (motion), and immunopharmacology (immunity).

Increased funding is requested to expand the support for the pharmacology-toxicology centers. For 1975, an amount of $6,500,000 for pharmacology-toxicology research centers is requested in order to support two or three additional centers.

The increase in fellowships will be utilized for support of postdoctoral individual fellowship awards in clinical pharmacology and toxicology. Both of these areas are identified as having current critical shortages of research-trained individuals.

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* Excludes 1973 appropriation restorations.

Current Program:

The objective of the Pharmacology-Toxicology Program is to improve medical therapy through increased understanding of the mechanisms of drug action, and how this action is influenced by various factors, such as genetic differences among patients and concomitant administration of other drugs. Research supported by this program is providing a rational basis for the safer use of presently available drugs and is contributing to the design of more effective therapeutic agents.

The program's efforts in dermatopharmacology seek more efficacious drugs for treatment of serious, sometimes fatal, skin disorders. Many skin diseases also involve a variety of other organs, such as the cardiovascular, respiratory and skeletal systems. An example of research in this area is a program currently funded at Brown University. Investigators on this grant have developed a new drug which appears to be effective in serious cases of psoriasis. While this disease is usually mild, it can progress to a very serious state involving grossly deforming skin lesions over the entire body, a severe form of arthritis, cardiovascular disease, and marked muscle wasting.

Inherited variations in individuals may produce important differences in duration and intensity of a drug's effect. The duration of action of a commonly used muscle relaxant depends on a serum enzyme which normally terminates the drug's action. Certain genetic variants of this enzyme are much less effective, causing the drug to persist for a dangerously long period of time. By use of recently developed methods it is now possible to separate normal and atypical variants and to identify individuals with these genetic differences before exposure to the drug.

Simpler, more specific and sensitive instruments are being developed to permit selective analysis of the minute quantities of drugs and their metabolites found in blood and tissues after therapeutic doses. These studies should lead to automated procedures which are suitable for monitoring blood levels of drugs and for detecting inadvertent drug ingestion and narcotics.

A cooperative effort with the Atomic Energy Commission has permitted the increased production of drugs labeled with non-radioactive stable isotopes of carbon, oxygen, nitrogen, and sulfur. Such drugs as dilantin, phenobarbital, and progestational steroids are being synthesized and labeled with carbon-13 for pediatric and perinatal pharmacology research that was not previously possible with radioactive labels.

The Research Triangle Institute (RTI) is completing work, supported under a contract, on the oral contraceptive steroids. Because of the controversial use of diethylstilbestrol (DES) as a drug and as a former fattening agent for cattle, the RTI has been studying the isoflavin analog of this drug which exhibits hormonal properties without apparent change in breast tissue from normal to tumorous state. A sensitive, inexpensive radioimmunoassay procedure has been developed for a widely used anticonvulsant drug. The usefulness of the RTI test has been confirmed by several epilepsy centers. The Research Triangle Institute is also collaborating with NIGMS grantees in special drug syntheses and analyses when these would ordinarily be unavailable.

The Boston Collaborative Drug Surveillance Program (BCDSP), under contract with the NIGMS, has continued to improve the methodology for predicting and detecting adverse drug reactions, and for more accurate determination of drug efficacy for specific diseases. Two highly interesting findings have been reported in preliminary form. The first is an apparent decrease in the number of fatal heart attacks among chronic users of aspirin. Whether this is due directly to the aspirin or to associated factors has not yet been determined. The other preliminary finding is the increase in heart attacks among patients ingesting four to five cups of coffee daily as compared with those drinking less or with those drinking no coffee. The investigators feel that this effect is not due to caffeine, since an increased incidence of heart attacks was not observed in individuals consuming similar amounts of tea.

Biomedical Engineering

Authorizing Legislation: Public Health Service Act, Title IV, Part E

	1974 Base *		1975 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits	---	---	---	---	---	---
Other expenses	---	$21,470,000	---	$21,421,000	---	-$49,000
Total	---	21,470,000	---	21,421,000	---	-49,000
Budget Mechanism:						
Research Grants:						
Regular program	---	11,864,000	---	11,683,000	---	-181,000
Special Programs:						
Diagnostic Radiology Centers	---	891,000	---	972,000	---	+81,000
Biomedical Engineering Centers	---	1,425,000	---	2,000,000	---	+575,000
Research Career	---	460,000	---	426,000	---	-34,000
Scientific Evaluation	---	60,000	---	68,000	---	+8,000
Subtotal Special	---	2,836,000	---	3,466,000	---	+630,000
Fellowships	---	1,094,000	---	1,595,000	---	+501,000
Training Grants	---	4,176,000	---	3,399,000	---	-777,000
Research & Development Contracts	---	1,500,000	---	1,278,000	---	-222,000
Total	---	21,470,000	---	21,421,000	---	-49,000

Plans in F.Y. 1975

The ongoing program of research grants, diagnostic radiology centers, training grants, fellowships, and research and development contracts will be pursued vigorously, with increases or special emphasis in the following areas: application of engineering control theory to the study of physiological processes, computer-aided clinical decision making, and use of ultra-sound, infrared and laser radiation for improvement of diagnostic radiology.

In response to Congressional interest, the Institute has initiated a Biomedical Engineering Centers Program. The requested amount of $2,000,000 for Biomedical Engineering Centers would provide for the establishment of five or six centers by the end of 1975.

Research emphasis in the area of Automation of the Clinical Laboragory will be on: more accurate methods for the determination of blood constituents, reliable specimen identification, and automated cytology techniques.

Special attention will be devoted to support of postdoctoral research training in Clinical Laboratory Science and Diagnostic Radiology.

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* Excludes 1973 appropriation restorations.

Research and development contracts will be sought in the following areas: automation in microbiology, electrolyte measurement in body fluids, software for small computers for clinical laboratories, ultratrace metal analyses, automated cell analyzer, and automated reticulocyte blood cell counter.

Current Program

The main objectives of the Biomedical Engineering Program are to support the effective introduction of the principles and practice of engineering science into fundamental and applied biomedical research, and to support quality research training in the area. In selected instances, prototype instrumentation and devices are developed that will be useful in improvement of health care.

Research support is provided for theoretical, developmental, and applied aspects of biomedical instrumentation, biomaterials, computers in biomedical research, and application of physical science and engineering principles in health care. An example of this type of research deals with computer-aided image recognition, which can assist the diagnostic radiologist in identifying hard-to-see images, such as lung tumors on chest X-rays. Presently, up to 25 percent of such images may be missed, even by highly trained diagnosticians. An Institute-supported project at the University of California-Irvine is developing a highly sensitive electronic scanner for detection of slight variations of density on the X-ray. Output is then coupled to a computer to correct out the background images produced by the overlay of ribs, blood vessels and other tissue, and to produce, thereby, a clearer outline of the tumor image.

An overall goal is to develop a modular automated clinical laboratory system that can be adapted to benefit all sizes of hospitals from the small community hospital to the large university hospital complex. The GeMSAEC fast centrifugal analyzer, developed under NIGMS support at the Oak Ridge National Laboratory, has now been miniaturized into a system weighing 20 pounds and requiring only a cubic foot of space. This compact table-top model needs only a few microliters of blood, urine, or other body fluid samples for each chemical assay, and is ideal for use at the bedside, in remote areas, or in small clinics. The GeMSAEC principle is being extended to even smaller battery powered units for mobile or emergency use.

Georgetown University and the American Science and Engineering Company are collaborating in developing a unique working system for reliable laboratory sample identification. The system is aimed at solving a major problem in the clinical laboratory, which is the proper matching of specimens with the patients from whom they were obtained.

The increasing availability of anti-viral therapeutic agents has highlighted the need for rapid and economical methods of isolating and specifically identifying viral specimens. Two new techniques, both based on immunological principles, are being actively investigated, under contract support.

Clinical and Physiological Sciences

Authorizing Legislation: Public Health Service Act, Title IV, Part E

	1974 Base *		1975 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits...........	---	---	---	---	---	---
Other expenses...........	---	$21,138,000	---	$23,251,000	---	+$2,113,000
Total..........	---	21,138,000	---	23,251,000	---	+2,113,000

Budget Mechanism:

	Pos.	Amount	Pos.	Amount	Pos.	Amount
Research Grants:						
Regular program......	---	4,978,000	---	4,902,000	---	-76,000
Special program:						
Anesthesiology Research Centers.	---	1,199,000	---	3,028,000	---	+1,829,000
Trauma Centers.....	---	1,900,000	---	5,000,000	---	+3,100,000
Research Career....	---	320,000	---	329,000	---	+9,000
Scientific Evaluation.......	---	10,000	---	19,000	---	+9,000
Subtotal Special	---	3,429,000	---	8,376,000	---	+4,947,000
Fellowships............	---	1,806,000	---	1,081,000	---	-725,000
Training Grants........	---	10,925,000	---	8,892,000	---	-2,033,000
Total..........	---	21,138,000	---	23,251,000	---	+2,113,000

Plans in F.Y. 1975

The ongoing program of research grants, anesthesiology and trauma centers, training grants, and fellowships will be pursued vigorously, with increases or special emphasis in the following areas: this program was recently reorganized to encompass the areas of anesthesiology, trauma research, general medicine, and adaptation and behavior. Research in anesthesiology, especially in new approaches for the control of pain, will actively be stimulated by the Institute. Many of the opportunities were pointed out by an International Pain Symposium in May 1973, funded in part by the NIGMS. Increased support will be provided for activities at the Anesthesiology Research Centers. An amount of $4,000,000 is requested for support of two or three additional Centers in 1975. The role of acupuncture in surgical anesthesia and in relief of chronic pain will continue to be explored through discussion forums and through research grant support.

Trauma research will receive increased support. For 1975, an amount of $5,000,000 is requested in order to support six or seven additional Trauma Centers. A workshop, sponsored by the NIGMS in February 1973 considered current challenges facing the Trauma Program. A number of research opportunities became evident, for which follow-up is planned: basic mechanisms for the sequential failure of organ systems in shock, involving successively the cardiovascular, renal, pulmonary, and nervous systems; a wide array of blood problems, ranging from preservation, regeneration, and blood substitutes, to immune mechanisms and the reasons for hemolysis and anemias following burns; aspects of wound healing,

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* Excludes 1973 appropriation restorations.

such as fibrosis, wound contraction, and scar tissue remodeling, which affect rate and success of healing; and immunological problems, both long-term immune responses and various short-term antibacterial mechanisms.

A further stimulus to trauma research is the interest expressed by Congress in fire prevention and control (e.g., Federal Fire Prevention and Control Act, S. 1769 and H.R. 11895). The Institute is providing increased support for research relevant to treatment of fire and burn victims.

The Institute has identified trauma research, epidemiology, anesthesiology, and behavioral science as four areas critically short in research-trained manpower, and postdoctoral fellowship awards in these areas will be emphasized. Physiology and surgery constitute other disciplines in which research training should continue to be supported to avoid future shortages.

Trauma Research

The goal in this training area is to educate individuals capable of advancing our knowledge of the body's complex reactions to trauma. Candidates are expected to emphasize research training in such fields as physiology or biochemistry and should be under the supervision of a staff that includes both trauma surgeons and basic scientists.

Epidemiology

Demands for epidemiologists have been significantly increased as investigators focus increasingly on chronic diseases which present them with new types of incidence, distribution, and control of disease problems. Other new epidemiologic fields deal with the environment and the utilization and evaluation of health care.

Anesthesiology

This is considered one of the undermanned medical specialties, and the shortage of research-trained medical faculty is particularly serious. Knowledge of the effects of anesthetic agents on the brain is very limited. This ignorance includes the basic mechanism of action of gas anesthetics, as well as the concomitant effects on, for instance, the vascular system. The basic nature of pain remains unknown. The anesthesiologist with thorough research training is the most likely to make advances in these areas.

Behavioral Science

There is a growing acceptance that behavioral scientists are an essential part of the research, teaching, and practice of medicine. Research done in a medical setting by behavioral scientists is more likely to have an impact on health than that done in isolation. The supply of suitably trained candidates for faculty positions is grossly inadequate and needs to be stimulated.

Current Program

The specific objectives of the Anesthesiology segment are to support basic and clinical research in anesthesia as a basis for improved care to patients requiring surgical procedures, respiratory assistance, or relief from chronic pain. The program includes research on the use of anesthetic agents, basic physiologic and metabolic changes from anesthetics, management of respiratory failure, resuscitation, and intensive care. The NIGMS currently supports three centers in anesthesia research.

An example of research at such a center: respiratory distress syndrome (RDS), a serious problem in newborn children. Findings obtained at the Columbia University

Anesthesiology Research Center, using animal models of the disease, have pointed towards surgical intervention as a possible beneficial mode of corrective treatment.

At the International Pain Symposium in Seattle, sixty active scientists from many countries assembled to report new information and to exchange ideas on pain. The symposium stimulated a number of participants to collaborate with colleagues in other disciplines in new approaches to research on pain.

The specific objectives of the Trauma segment are to discover better ways to prevent death from injury, alleviate pain, speed recovery of patients, and lessen the degree of disability caused by injuries. Trauma, from whatever cause, is a complex "disease" which can result in the greatly feared after effects of sequential organ failure. Many of the problems of trauma require exploration in depth at the biochemical and physiologic level, and require both basic scientists and clinical investigators. In the trauma research centers, these problems are being attacked through studies of metabolic changes, respiratory failure, fluid imbalance, and severe infections which frequently follow severe injury. Improved methods of management developed through such research have enabled the successful treatment of 85 percent of patients who enter the centers.

The NIGMS continues to support research on the mechanism of acupuncture. During an acupuncture research conference sponsored by the NIGMS in 1973, scientists in the fields of anesthesiology, neurology, neurophysiology and psychology reported on their current research. The proceedings from this meeting have been published. Based on results presented at the conference, the NIH Advisory Committee on Acupuncture concluded that acupuncture produces definite effects of interest and that it holds some promise as an anesthetic for some surgical operations and for the treatment of some acute and chronic painful conditions. While it is not yet known how acupuncture works or how well it compares with other established procedures for treating pain, it was agreed that many more well-designed and well-controlled studies are needed before it could be considered for wide use in clinical practice in the United States.

Genetics

Authorizing Legislation: Public Health Service Act, Title IV, Part E

	1974 Base *		1975 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits...........	---	---	---	---	---	---
Other expenses...........	---	$45,194,000	---	$46,087,000	---	+$893,000
Total..........	---	45,194,000	---	46,087,000	---	+893,000
Budget Mechanism:						
Research Grants:						
Regular program......	---	30,862,000	---	30,618,000	---	-244,000
Special programs:						
Genetic Research Centers..........	---	5,985,000	---	7,000,000	---	+1,015,000
Research Career....	---	2,825,000	---	2,314,000	---	-511,000
Scientific Eval....	---	67,000	---	101,000	---	+34,000
Subtotal Special.	---	8,877,000	---	9,415,000	---	+538,000
Fellowships............	---	2,143,000	---	3,582,000	---	+1,439,000
Training Grants........	---	2,498,000	---	2,033,000	---	-465,000
Research & Development Contracts............	---	814,000	---	439,000	---	-375,000
Total..........	---	45,194,000	---	46,087,000	---	+893,000

Plans in F.Y. 1975

The ongoing program of research grants, genetic centers, training grants, fellowships, and research and development contracts will be pursued vigorously, with increases or special emphasis in the following areas: uncovering of the basic lesions responsible for genetic disease, preventive technology, tissue culture studies of mammalian systems, and techniques for early identification of individuals destined to suffer late-onset genetic illness, such as Huntington's disease.

The Institute will evaluate applications for Genetic Research Centers for possible funding. In addition, high-quality program project grants based on logical team efforts in genetics will be encouraged. Such efforts would combine the talents and resources of a group of investigators working in a common area.

The program will also continue to explore ways for stimulating research into the ethical, legal, and social aspects of genetic counseling and screening. How well are these procedures accepted; how can they be improved to better serve a concerned population? A conference on this subject is under consideration.

Research training in Medical Genetics will receive special emphasis through fellowship awards. Medical geneticists will have variable backgrounds, some with graduate training in basic genetics with postdoctoral training in departments of

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* Excludes 1973 appropriation restorations.

human genetics, others with the M.D. background who will need thorough research training in basic genetics.

Current Program:

The Genetics Program is directed toward gaining a better understanding of the fundamental processes and mechanisms of inheritance in health and disease. Its objectives are the prevention, therapy and cure of genetic ills in man, including multifactorial diseases with a strong hereditary component, such as diabetes, atherosclerosis, hypertension, and schizophrenia. The various categorical NIH Institutes appropriately consider the treatment of individual diseases as discrete problems requiring a specific approach and resolution. In contrast, the NIGMS Genetics Program attempts to exploit broadly strategic research opportunities which may yield generalizable concepts.

The eight Genetic Centers, one of which was initiated in F.Y. 1973, combine basic research with clinical application and provide excellent settings for the clinical evaluation of new findings through their involvement in genetic community services, such as counseling. For example, researchers at the Genetic Center at the University of Washington have contributed to our understanding of the hereditary aspects of several serious diseases. They demonstrated the genetic aspects of three common lipid disorders (hypercholesterolemia, hypertriglyceridemia, and combined hyperlipidemia) which are predisposing factors in heart attacks. The genes playing a role in these disorders may well be the most prevalent disease-producing genes within the American population, for the three lipid disorders together account for fully one-fifth of all acute coronary episodes in patients up to age 60. They have also shown the feasibility of screening for early identification of individuals at risk which would permit prompt institution of preventive measures such as dietary control, drug therapy, or changes in life style. This genetic center is also conducting research into the control of sickle cell anemia, through basic studies of the genes responsible for producing the abnormal sickle cell hemoglobin, and of biochemical methods for treating red cells to reduce their tendency to clump together within the small blood vessels in the body. A promising system has been devised for shunting blood from sickle cell patients outside the body where it is exposed to cyanate, then excess cyanate removed by dialysis, and finally the cyanate-treated cells reinfused into the body. This method for treatment with cyanate or perhaps other anti-sickling agents reduces the danger of deleterious side effects from drug therapy.

The NIGMS supports, through contract, the operation of a Human Mutant Cell Repository for collection, storage, and distribution of cultures of normal and genetic mutant human cells. The overall objective is to facilitate and support expanded clinical and basic research in human genetics.

Cellular and Molecular Basis of Disease

Authorizing Legislation: Public Health Service Act, Title IV, Part E

	1974 Base *		1975 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits...........	---	---	---	---	---	---
Other expenses...........	---	$47,824,000	---	$44,925,000	---	-$2,899,000
Total..........	---	47,824,000	---	44,925,000	---	-2,899,000
Budget Mechanism:						
Research Grants:						
Regular program......	---	25,054,000	---	24,673,000	---	-381,000
Special programs:						
Molecular Pathology Centers..........	---	475,000	---	500,000	---	+25,000
Research Career....	---	2,951,000	---	2,405,000	---	-546,000
Scientific Evaluation.......	---	109,000	---	116,000	---	+7,000
Subtotal Special	---	3,535,000	---	3,021,000	---	-514,000
Fellowships.............	---	3,016,000	---	4,028,000	---	+1,012,000
Training Grants........	---	16,219,000	---	13,203,000	---	-3,016,000
Total...........	---	47,824,000	---	44,925,000	---	-2,899,000

Plans in F.Y. 1975

The ongoing program of research grants, training grants, and fellowships will be pursued vigorously, with increases or special emphasis in the following areas: one promising initiative, encouraged by the Congress last year, is the establishment of Molecular Pathology Centers, which bring together cellular and molecular scientists with pathologists and clinical investigators to perform research on membranes, subcellular particles (organelles) and on their role in disease. An amount of $500,000 is requested to provide continuing support for the one Molecular Pathology Center we expect to fund by the end of 1974.

Special emphasis will be made to provide opportunities at the postdoctoral level, through fellowship awards, for advanced training in Pathology of Membranes and Organelles, regarded as an area of high program priority and significant manpower shortage, as specially trained researchers are needed to focus on the pathology of the cell described in subcellular and molecular terms. The Cellular and Molecular Basis of Disease Program will also continue an active program in support of basic research training in a number of areas, including anatomical sciences, cell biology, biochemistry, biophysical sciences, and microbiology. Of special importance is the support of training in emerging fields which are usually interdisciplinary in nature. In one such program, graduate study is coupled specifically with the study of medicine.

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* Excludes 1973 appropriation restorations.

Current Program

The Cellular and Molecular Basis of Disease Program deals at the fundamental science level with the structure and function of the cellular machinery common to all living organisms. Basic knowledge is sought about how the subunits of cells participate in the many activities which are coordinated so smoothly in health, but which become deranged and in disarray in disease. The development of a general pathology of cells, their membranes, organelles, and molecular constituents has become an essential step in the study of disease, and is an important goal of this program. Physicians of the future may well look at cellular abnormalities for important clues in characterizing and analyzing illnesses previously described at the organ level, such as heart or kidney disease. Because of its roots in the fundamental sciences, this--of all the NIGMS programs--has been most dependent upon the contributions of creative, curiosity-oriented investigators.

Research Management and Program Services

Authorizing Legislation: Public Health Service Act, Title IV, Part E

	1974 Base *		1975 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits..........	155	$2,733,000	155	$2,734,000	---	+$1,000
Other expenses..........	---	3,792,000	---	3,736,000	---	-56,000
Total.........	155	6,525,000	155	6,470,000	---	-55,000
Budget Mechanism:						
Research Management and Program Services.	155	6,525,000	155	6,470,000	---	-55,000
Total..........	155	6,525,000	155	6,470,000	---	-55,000

This program provides for the overall leadership and staffing necessary for the administration and management of the research effort of the Institute and supports the National Advisory General Medical Sciences Council. In 1975, the professional and supporting staff will continue to maintain close surveillance and guidance required for the many programs of the Institute.

The net decrease of $55,000 reflects a built-in increase of $139,000 offset by a built-in decrease of $75,000 for savings resulting from annualization of the 1974 employment reduction and a decrease of $119,000 in the payment to the NIH Management Fund for centrally furnished services.

The built-in increase of $139,000 includes the following: $30,000 for within-grade pay increase costs, $11,000 for an extra day of pay in 1975, $20,000 for increased costs of using the Federal Telecommunications System, $41,000 for increased costs charged through the NIH Service and Supply Fund, $1,000 for the Bureau of Employment Compensation rate increases, and $36,000 for annualization costs of the October 1973 pay raise.

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* Excludes 1973 appropriation restorations.

NATIONAL INSTITUTES OF HEALTH

National Institute of General Medical Sciences

Program Purpose and Accomplishments

Activity: Pharmacology-Toxicology (Public Health Service Act, Title IV, Part E)

1974			1975 Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
---	$24,654,000	Indefinite	---	$26,175,000

Purpose: The purpose of the pharmacology-toxicology program is to improve medical therapy through acquisition of increased knowledge of the mechanisms of drug action, of ways to increase efficacy and safety, and to diminish toxicity.

Explanation: This program supports research through regular research grants, special center grants, fellowships, training grants, and contracts. This program also funds direct training for 18 intramural NIH "research associates."

Accomplishments, 1973/1974: A total of 441 research grants, centers, fellowships, and training grants and five contracts were funded in 1973. Research in enzymatic metabolism, body distribution, and excretion of drugs will be pursued on a broad front. Applications of sophisticated new analytical techniques, such as gas chromatography - mass spectrometry, use of compounds labeled with stable isotopes, and radio-immuno assay, will accelerate progress in these areas. Computer technology and the skills of synthetic bio-organic chemists will be applied to efforts to develop improved therapeutic agents. A new training program for postdoctoral candidates will be initiated in 1974.

Objectives, 1975: Unifying principles established through basic research will be further applied to problems in therapy. Emphasis will be devoted to emerging opportunities, especially in pharmacogenetics, immunopharmacology, pharmacokinetics, and dermatopharmacology. A continuing effort will be made to assess the risks from adverse drug reaction and from drug-drug interactions, as well as to determine the efficacy of commonly utilized drugs. Additional emphasis will be given to the activities encompassed within the pharmacology-toxicology centers.

NATIONAL INSTITUTES OF HEALTH

National Institute of General Medical Sciences

Program Purpose and Accomplishments

Activity: Biomedical Engineering (Public Health Service Act, Title IV, Part E)

1974			1975	
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
---	$21,470,000	Indefinite	---	$21,421,000

Purpose: The purpose of the biomedical engineering program is to support the effective introduction of engineering science into fundamental and applied biomedical research. Prototype instrumentation and devices are being developed that will be useful in the improvement of health care.

Explanation: This program supports research through regular research grants and special center grants. Contracts are utilized for the support of applied research and development. A number of individuals in clinical chemistry, biomedical engineering, and diagnostic radiology have been and are currently being supported through fellowships and training grants.

Accomplishments, 1973/1974: This program was supported by a total of 206 research grants, centers, fellowships, training grants, and seven contracts in 1973. Research includes the development of systems for rapid data acquisition and display, involving new types of transducers and integrated electronic circuitry. Emphasis will continue on instruments for positive patient/sample identification, for automated laboratory procedures, and newer techniques in diagnostic radiology. A new training program for postdoctoral candidates will be initiated in 1974.

Objectives, 1975: Improved automated systems will be conceptualized and research stimulated on their development. One or two new biomedical engineering centers will be initiated and developed in 1975. These centers will provide a focal point where optimal interdisciplinary interaction can take place between physicians, scientists, and engineers. Emphasis will be placed on the application of engineering control theory to the study of physiological processes, computer-aided clinical decision making, and use of ultra-sound, infrared and laser radiation for improvement of diagnostic radiology. These centers will require the development of prototype university patterns and new institutional forms that are appropriate for advancing the integration of knowledge between engineering and biomedicine.

NATIONAL INSTITUTES OF HEALTH

National Institute of General Medical Sciences

Program Purpose and Accomplishments

Activity: Clinical and Physiological Sciences (Public Health Service Act, Title IV, Part E)

1974		1975		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
---	$21,138,000	Indefinite	---	$23,251,000

Purpose: The purpose of the clinical and physiological sciences program is to promote and foster basic and clinical research in the physiological sciences and in certain clinical areas, particularly anesthesiology and trauma.

Explanation: This program supports research through regular research grants, special center grants, as well as fellowships and training grants.

Accomplishments, 1973/1974: This program was supported by a total of 232 research grants, centers, fellowships, and training grants in 1973. The Institute has begun to explore its role in the support of research on acupuncture in surgical anesthesia and in relief of chronic pain. The increasing involvement of anesthesiologists in the total respiratory care of patients is the stimulus for developing improved methodologies and devices for diagnosis and treatment of hypoxia, complications from anesthesia, and cerebral vascular insufficiencies. The effectiveness of acupuncture in surgical anesthesia and in relief of chronic pain will be further explored. Many aspects of wound healing, mechanisms of shock, and other factors related to trauma will be supported. A new training program for postdoctoral candidates will be initiated in 1974.

Objectives, 1975: A number of research opportunities have been identified by Institute staff and consultants in recent workshop conferences. Research will be extended into these basic physiologic and applied clinical areas--including studies of pain and its control, resuscitation, effects of drowning, the molecular basis of anesthesia, sequential organ failure in shock, blood problems, and instrumentation for trauma diagnosis and therapy. Several new research centers in anesthesiology and trauma will be initiated and developed.

NATIONAL INSTITUTES OF HEALTH

National Institute of General Medical Sciences

Program Purpose and Accomplishments

Activity: Genetics (Public Health Service Act, Title IV, Part E)

1974			1975 Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
---	$45,194,000	Indefinite	---	$46,087,000

Purpose: The purpose of the genetics program is to support research aimed at the prevention, therapy, and control of genetic diseases in man, including those multifactorial illnesses with a strong hereditary component.

Explanation: Genetic research is supported through regular research grants, centers, training grants, fellowships, and contracts. The NIGMS approaches the problem of human genetic disease as a generalized phenomenon involving common mechanisms, and amenable to elucidation on the basis of a broad fundamental research approach.

Accomplishments, 1973/1974: The genetics program was supported in 1973 by a total of 829 research grants, centers, fellowships, training grants, and four contracts. Particular attention will be devoted to genetic mapping of the human chromosome, identification of carriers of genetic disease, and control mechanisms for genetic expression in man. The contract-supported "Human Genetic Mutant Cell Repository" will provide seed stocks of well-characterized human tissue culture cells to researchers in the field. A new training program for postdoctoral candidates will be initiated in 1974.

Objectives, 1975: Attention will be given to monitoring some of the newer approaches to treatment of genetic disease, with encouragement of support for methodologies which appear scientifically sound and justified. Continued emphasis will be placed on the development of genetic research centers, with several new centers being initiated. Special emphasis will be given to: uncovering of the basic lesions responsible for genetic disease, preventive technology, tissue culture studies of mammalian systems, and techniques for early identification of individuals destined to suffer late-onset genetic illness, such as Huntington's disease.

NATIONAL INSTITUTES OF HEALTH

National Institute of General Medical Sciences

Program Purpose and Accomplishments

Activity: Cellular and Molecular Basis of Disease (Public Health Service Act, Title IV, Part E)

1974			1975	
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
---	$47,824,000	Indefinite	---	$44,925,000

Purpose: The purpose of the cellular and molecular basis of disease program is to support research on the structure and function of human cells and their component parts, with the expectation that a greater understanding of these aspects will contribute to ultimate control of all forms and manifestations of disease.

Explanation: This program supports research through regular research grants, centers, fellowships, and training grants.

Accomplishments, 1973/1974: This program was supported by a total of 926 research grants, fellowships, and training grants in 1973. Research support in the fields of anatomical sciences, biochemistry, biophysics, microbiology, and pathology will contribute to the goals of this program. Research encompasses detailed studies of the structure of cellular organelles, their function under normal and diseased conditions, and responses to injury and aging. Enormous advances have been made recently in our understanding of the chemical structure of cell membranes, their microscopic appearance, and their manifold functions, including the highly selective transport of material in solution from outside the cell, and vice versa. The base of knowledge in cell biology will be broadened by molecular studies of proteins, metabolic reactions, and cell transport. A new training program for postdoctoral candidates will be reinstituted in 1974.

Objectives, 1975: Research in cell differentiation and specialization will be emphasized. Newer instruments for investigating cell structure, such as the high voltage scanning electron microscope, will be exploited for the study of membranes and other subcellular components.

NATIONAL INSTITUTES OF HEALTH

National Institute of General Medical Sciences

Program Purpose and Accomplishments

Activity: Research Management and Program Services (Public Health Service Act, Title IV, Part E)

1974			1975	
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
155	$6,525,000	Indefinite	155	$6,470,000

Purpose: This program provides for the overall leadership and staffing necessary for the administration and management of the research effort of the Institute and supports the National Advisory General Medical Sciences Council.

Explanation: The National Institute of General Medical Sciences supports a broad base of fundamental and applied biomedical research programs aimed at the solution of certain major health problems. The Institute Director and his staff are responsible for the overall direction, planning, and evaluation of these programs.

Accomplishments, 1973/1974: The Director and supporting professional and clerical staff provided continuing guidance and surveillance over the pharmacology-toxicology, engineering in biology and medicine, clinical and physiological sciences, genetics, and cellular and molecular basis of disease programs of the Institute. A total of 2,634 research grants, special center grants, fellowships, training grants, and 16 research contracts were funded in 1973. It is estimated that approximately 2,796 grants and fellowships and 12 research contracts will be funded in 1974.

Objectives, 1975: In 1975, the professional and supporting staff will continue to maintain close surveillance and guidance required for the many programs of the Institute.

THURSDAY, MARCH 28, 1974.

NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT

WITNESSES

DR. PHILIP A. CORFMAN, DIRECTOR, CENTER FOR POPULATION RESEARCH, AND ACTING DIRECTOR, NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT

DR. DeWITT STETTEN, JR., DEPUTY DIRECTOR FOR SCIENCE, NATIONAL INSTITUTES OF HEALTH

DR. CHARLES LOWE, SCIENTIFIC DIRECTOR, NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT

JOEL R. HEDETNIEMI, EXECUTIVE OFFICER, NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT

DALE D. DeWALD, ACTING FINANCIAL MANAGEMENT OFFICER, NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT

LELAND B. MAY, ACTING DIRECTOR OF FINANCIAL MANAGEMENT, NATIONAL INSTITUTES OF HEALTH

WILFORD J. FORBUSH, DIRECTOR, DIVISION OF BUDGET FORMULATION, DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

Object Classification (in thousands of dollars)

Identification code 09-25-0844-0-1-651		1973 actual	1974 est.	1975 est.
	Direct obligations:			
	Personnel compensation:			
11.1	Permanent positions	7,795	8,812	9,328
11.3	Positions other than permanent	780	825	840
11.5	Other personnel compensation	155	167	180
	Total personnel compensation	8,730	9,804	10,348
12.1	Personnel benefits: Civilian	974	1,081	1,130
21.0	Travel and transportation of persons	384	385	395
22.0	Transportation of things	86	86	95
23.0	Rent, communications, and utilities	466	516	400
24.0	Printing and reproduction	145	145	150
25.0	Other services	26,388	29,367	28,710
26.0	Supplies and materials	1,313	1,410	1,499
31.0	Equipment	601	775	750
41.0	Grants, subsidies, and contributions	72,120	100,541	81,420
	Total direct obligations	111,207	144,110	124,897
	Reimbursable obligations:			
21.0	Travel and transportation of persons	1	5	5
25.0	Other services	---------	40	40
	Total reimbursable obligations	1	45	45
99.0	Total obligations	111,208	144,155	124,942

Personnel Summary

	1973 actual	1974 est.	1975 est.
Total number of permanent positions	563	521	529
Full-time equivalent of other positions	84	84	84
Average paid employment	593	602	608
Average GS grade	8.5	8.6	8.6
Average GS salary	$14,260	$15,138	$15,473
Average salary of ungraded positions	$11,138	$12,018	$12,253

Program and Financing (in thousands of dollars)

	Identification code 09-25-0844-0-1-651	1973 actual	1974 est.	1975 est.
	Program by activities:			
	Direct program:			
	1. Population	37,813	46,901	40,183
	2. Child health	50,980	61,906	52,378
	3. Aging	9,171	12,761	9,128
	4. Intramural, laboratory, and clinical research	13,891	14,228	14,683
	5. Research management and program services	7,092	8,314	8,525
	Total direct program	118,947	144,110	124,897
	Reimbursable program:			
	5. Research management and program services	1	45	45
	Total program costs, funded [1]	118,948	144,155	124,942
	Change in selected resources (undelivered orders)	−7,740	---------	---------
10	Total obligations	111,208	144,155	124,942
	Financing:			
	Receipts and reimbursements from:			
11	Federal sources	---------	−40	−40
14	Non-Federal sources	−1	−5	−5
25	Unobligated balance lapsing	19,243	---------	---------
	Unobligated balance restored	---------	−19,243	---------
	Budget authority	**130,450**	**124,867**	**124,897**
	Budget authority:			
40	Appropriation	130,429	130,254	124,897
	Withheld from obligation and expenditure (Public Law 93-192)	---------	−5,357	---------
41	Transferred to other accounts	---------	−30	---------
42	Transferred from other accounts	21	---------	---------
43	**Appropriation (adjusted)**	**130,450**	**124,867**	**124,897**
	Relation of obligations to outlays:			
71	Obligations incurred, net	111,207	144,110	124,897
72	Obligated balance, start of year	82,309	77,525	87,510
74	Obligated balance, end of year	−77,525	−87,510	−67,308
77	Adjustments in expired accounts	−1,273	---------	---------
90	Outlays	114,718	134,125	145,099

[1] Includes capital outlays as follows: 1973, $993 thousand; 1974, $775 thousand; 1975, $750 thousand.

NOTES

Excludes $73 thousand in 1975 for activities transferred to: Office of Assistant Secretary for Health, 1973, $73 thousand; 1974, $73 thousand.

Excludes $30 thousand in 1974 and 1975 for activities transferred to: Departmental Management. Comparable amount for 1973 ($30 thousand) is included above.

Includes $183 thousand in 1975 for activities previously financed from (in thousands of dollars):

	1973	*1974*
National Institute of General Medical Sciences	155	155
Departmental management	1	1

Mr. **Flood.** Now we have the National Institute of Child Health and Human Development. The presentation will be made by Dr. Philip A. Corfman, Director, Center for Population Research.

We will place your biographical sketch in the record, Doctor, at this point.

[The biographical sketch follows:]

Biographical Sketch

Name: Philip A. Corfman, M.D.

Position: Director, Center for Population Research, National Institute of Child Health and Human Development.

Birthplace and date: Berea, Ohio; July 19, 1926.

Education: Oberlin Colege, 1950, bachelor of arts, Harvard Medical School, 1954, doctor of medicine.

Experience: Present, Director, Center for Population Research, NICHD; 1967–68, Chairman, Public Health Service Population Committee; 1967–68, Assistant to the Director for Population Research, NICHD; 1966–67, Acting Program Director, Reproduction Program, NICHD; 1965–66, Program Associate for Population Research, Reproduction Program, NICHD; 1964–66, guest scientist, Navy Medical Research Institute, Bethesda, Md.; 1964–65, consultant in obstetrics and gynecology, Reproductive Biology Program, NICHD; 1963–64, assistant visiting obstetrician and gynecologist, Harlem Hospital; 1963–64; visiting fellow, Vanderbilt Clinic, Columbia-Presbyterian Hospital; 1962–63, member, Medical Executive Committee, Rip Van Winkle Foundation; 1960–63, attending obstetrician, Columbia Memorial Hospital, Hudson, N.Y.; 1959–63, obstetrician and gynecologist, Rip Van Winkle Clinic, Hudson, N.Y.; 1956–59, obstetricial and gynecological residency, Boston Lying-In Hospital and the Free Hospital for Women; 1956–59, teaching fellow in obstetrics and gynecology, Harvard Medical School; 1954–56, surgical internship and first year residency, Boston City Hospital, Fifth Surgical Service (Harvard).

Professional societies: American Board of Obstetrics and Gynecology; American College of Obstetricians and Gynecologists; Food and Drug Administration Advisory Committee on Obstetrics and Gynecology; Population Association of America; Society for the Study of Fertility; World Health Organization Advisory Group to the Expanded Programme of Research, Development and Research Training in Human Reproduction.

Publications: Various publications on the development of contraceptives, cancer etiology, and cytogenetics.

Biographical Sketch

Name: Charles Upton Lowe, M.D.

Position: Scientific Director, National Institute of Child Health and Human Development.

Birthplace and date: Pelham, N.Y., August 24, 1921.

Education: Harvard University, 1942, bachelor of science, Yale Medical School, 1945, doctor of medicine.

Experience: Present, Scientific Director, NICHD; 1965–68, Director, Human Development Center and professor of pediatrics, University of Florida; 1951–65, Attending physician and Director of Research Children's Hospital, Buffalo; 1956–65, Buswell fellow and research professor of pediatrics University of Buffalo; 1951–56, associate professor of pediatrics, University of Buffalo; 1950–51, assistant professor of pediatrics, University of Minnesota; 1948–50, National Research Council Fellow, University of Minnesota; 1948, chief resident, Massachusetts General Hospital; 1947–48, assistant resident, Massachusetts General Hospital; 1947, Blackfan Memorial Fellow, Children's Hospital, Boston; 1946–47, resident, Children's Hospital, Boston; 1945–46, pediatric intern, Children's Hospital, Boston.

Professional societies: American Academy of Pediatrics, American Association for the Advancement of Science, American Association of University Professors, American Pediatric Society, American Institute of Nutrition, American Society for Clinical Investigation, American Society for Clinical Nutrition president (1969–70), American Society for Experimental Pathology, New York Academy of Sciences, Perinatal Research Society, Sigma Xi, Society for Experimental Biology and Medicine, Society for Pediatric Research, The Gerontological Society, The Royal Society of Medicine, London.

Biographical Sketch

Name: Joel R. Hedetniemi.

Position: Executive officer, National Institute of Child Health and Human Development.

Birthplace and date: Washington, D.C., August 23, 1940.

Education: The George Washington University, 1962, B.A., The George Washington University, 1967, M.A.

Experience: Present. Executive Officer, National Institute of Child Health and Human Development; 1969–73, Executive Officer, Division of Allied Health Manpower, Bureau of Health Manpower Education, NIH; 1968–69, acting Executive Officer, Division of Allied Health Manpower, Bureau of Health Manpower Education, NIH; 1967–68, Program Management Officer, Division of Allied Health Manpower, Bureau of Health Manpower Education, NIH; 1966–67, Administrative Officer, National Institute of Mental Health, NIH; 1965–66, budget analyst, National Institute of Mental Health, NIH; 1963–65, management analyst, National Institute of Mental Health, NIH; 1962–63, management intern, National Institutes of Health.

Mr. Flood. Who do you want to introduce?

Dr. Corfman. Mr. Joel Hedetniemi, the Executive Officer, and Dr. Charles Lowe, the Scientific Director of the National Institute of Child Health and Human Development.

Mr. Flood. I see you have a statement. How do you want to handle it?

Dr. Corfman. I would be pleased to read it.

Mr. Flood. You may proceed.

Dr. Corfman. Please permit me to say in introduction that as an obstetrician-gynecologist I am proud to testify for the Insttiute today. I believe this may be the first time someone from my specialty has spoken for an institute.

Mr. Flood. Any reason for it other than your availability?

Dr. Corfman. I am speaking as an obstetrician with pride in my specialty.

Mr. Flood. The record will show there actually is no Director of this Institute.

Dr. Corfman. You might say I am Acting Director.

Mr. Flood. Why didn't you say so? Everybody else has a star on their shoulder as Acting Director.

Dr. Corfman. I am pleased to be here regardless of lack of stars.

Mr. Flood. Go ahead.

Dr. Corfman. Mr. Chairman and members of the committee, I am pleased to appear before this committee to present the programs of the National Institute of Child Health and Human Development, where the mission is the study of life as a continuum rather than research on a particular disease or biologic system. It is through this life-span approach that our investigators attack some of the country's most important biomedical problems in child health, population, and aging.

It is recognized that pregnancy, infancy, childhood, adolescence, adulthood, and old age are not isolated phases of the life cycle, but are interrelated in significant ways. Circumstances of pregnancy and childhood presage adulthood, while the middle adult years affect the quality of life of the aged. We know that the health of a pregnant woman, the drugs she takes, the food she eats, her minor and chronic illnesses as well as environmental influences can have profound effects upon her baby, both before and after it is born. For example, one of our recent studies has shown that women poorly nourished before and during pregnancy often give birth to babies of low birth weight and therefore at higher risk of health problems. Parallel studies indicate that maternal nutritional supplementation can increase birth weight.

Within this framework of life-span research, the Institute is focusing on three major objectives.

Objective: To decrease infant mortality and reduce diseases and handicaps in childhood.

SUDDEN DEATH SYNDROME

One of the most tragic and baffling killers of infants is the sudden death syndrome. In much the way detectives unravel a mystery, scientists are tracking down clues to its causes. Ultimately, they seek to discover why each year about 7,500 to 10,000 apparently healthy infants die suddenly and unexplainably, usually in their sleep.

During the sleep cycle, normal infants and even animals periodically stop breathing for a few seconds at a time. This is referred to as a period of apnea. A grantee has identified some infants who, in addition to having these brief periods of apnea, also have episodes lasting 15 seconds or longer. Speculation is that these infants may be at high risk for sudden death. Observed in hospital while they slept, several such babies required resusciation to start breathing again. Studies supported by the Institute indicate that infection is not the primary cause of the sudden infant syndrome, although it may be contributory.

MONGOLISM

Down's syndrome or mongolism is a type of mental retardation affecting over 5,000 children born each year. Because 50 percent of all affected infants are born to mothers over 35 years of age, we have mounted an educational campaign to inform these women of their increased chance of having such a child; and of the availability of a procedure that will permit detection of the condition early in gestation.

In this technique, called amniocentesis, cells are withdrawn for study from the fluid surronding the baby within the uterus. The technique is used to diagnose numerous genetic disorders prior to birth. However, scientists recognize that there still is need for further investigation of the short- and long-term benefits and possible risks of this relatively new technique. The Institute has underway a prospective study of 1,000 women who had amniocentesis performed and 1,000 control women who did not. The first phase has just been completed and data analysis has begun. The results of this research will provide an evaluation of the safety of the procedure which will help physicians determine the extent to which it may safely be used in prenatal detection of genetic disease.

Following successful experiments in animals, Institute scientists in our developmental immunology branch have recently begun a clinical trial of a vaccine against the leading cause of bacterial meningitis in children, hemophilus influenzae type b. The organism is responsible for about 12,000 to 15,000 cases of meningitis in infants and young children annually. Approximately 20 to 50 percent of the disease victims who recover suffer disability, including mental retardation. This project could make significant inroads against the leading cause of acquired mental retardation.

INFANT MORTALITY AND MORBIDITY

This fall the Institute will expand its intramural program for the study of pregnancy and infant mortality and morbidity. Scientists will study, for example, maternal metabolic adaptations accomplished during pregnancy and delivery, the initiation of labor, and adaptation of the newborn to life outside the uterus. This expanded activity will be housed in a new facility within the NIH Clinical Center.

ADOLESCENCE

An important, but heretofore neglected aspect of life-span research is adolescence. Far too little is known about either the biological or behavioral aspects of this stage in a person's life. During the past year we have launched an expanded program on adolescent development.

For 1975, the NICHD budget includes $60,625,000 for support of research activities in child health.

Objective: To promote the day when every child is wanted and when parents will be able to plan the most optimal time for the birth of their children.

FAMILY PLANNING

A recent Institute study analyzing European data supports the hypothesis that unwanted pregnancy badly affects the individual child. This study of offspring of mothers twice denied abortion both at the initial request and appeal, indicates that being unwanted at birth is detrimental in a number of significant ways. When matched with control children, the unwanted children were breast-fed a shorter time, were ill or injured more frequently during preschool age, performed less well in school, and showed more abnormal personality traits.

If unwanted conceptions are to be avoided, it is necessary to make available safe, effective, and desirable contraceptives. Data from the two national fertility studies we have supported have shown that oral contraceptives at present are by far the most popular means of family planning in this country. Therefore, it is necessary to support additional research aimed at minimizing or eliminating the side effects of these drugs. One group of investigators discovered that oral contraceptives appear to alter the requirements for several vitamins and minerals. Biochemical studies indicate a fall in blood levels of certain essential food elements such as ascorbic acid, pyridoxine, riboflavin, and zinc in users.

The possibility that oral contraceptives may cause birth defects has been addressed directly by studying the frequency of chomosome breakage in white cells of users. Although some increase has been noted, the significance of these findings remains uncertain either for the individual or for her offspring in view of the fact that similar changes are observed after use of certain drugs and following virus infections. We are continuing to support research on this problem.

A followup of some 13,000 women enrolled in a study we are funding has shown a sixfold increase in risk of elevated blood pressure among women on the pill as compared with women using other contraceptives. While the high blood pressure is in part reversible, it is not yet known whether it can be reversed in time to protect against such known complications as stroke or heart disease. In this same study, women currently using oral contraceptives were found to have a higher incidence of urinary tract infection than those who had never used them. No relationship was found between duration of use and incidence of infection, but apparently the type of pill used was related.

We do not yet have any ideal contraceptives; accordingly, we are supporting a number of promising approaches. Progress has been made in developing a new type of intrauterine device. This is fashioned from reinforced silastic rubber in the form of a pouch which after insertion is expanded by fluid pressure and takes on the shape of the uterine cavity. This device is soft and pliable and can be inserted easily. Preliminary data indicate that it is better tolerated than the IUDs presently available and has a very low expulsion rate. Another feature of the device is that the fluid-filled cavity might be used as a reservoir for antifertility compounds, thus increasing its effectiveness.

Data from an Institute study of male contraceptive agents is encouraging. Scientists have found that the formation of sperm in the human male can be controlled through daily oral administration of a weak androgen—a male hormone—combined with a once-a-month injection of a potent androgen. Men using this method have reported no decline in libido, a common complaint with other drug methods.

The 1975 NICHD budget includes $45,874,000 for support of population activities.

Objective: To improve the physical and mental health of the middleaged and aged.

AGING RESEARCH

Since 1900, the average lifespan in this country has increased from 49 to 71 years. In addition, an ever-increasing percentage of our total population is made up of persons in the upper age groups. Our goal is to understand the biological and behavioral aspects of aging in an effort to help older people lead productive and enjoyable lives.

As part of this effort, the Institute is emphasizing the study of aging in women, particularly during and after the menopause. According to the 1970 census, there are about 27 million women in the United States over 50 years of age. The average woman of 50 lives about 28 years beyond menopause; therefore, studies of female biology after ovulation has ceased are of great importance. Research has shown that in addition to the estrogen produced by the ovaries of women during their reproductive years, there is another biologically less active form of estrogen produced by other tissues of the body. Recently one of our studies has shown that this source of estrogen continues and that its level even increases after the menopause. Investigators have also found that after the menopause conditions such as liver disease and obesity increase estrogen production. Such studies will provide a better understanding of these extra sources of estrogen and their nature and may help to explain why women differ in menopausal symptoms and why some women have a greater need for replacement therapy than others.

Older persons are known to have a higher incidence of many diseases including heart disease, diabetes, cancer, and stroke. If risk factors leading to these serious disorders can be identified early when measures could be taken against them, the lives of older persons will be made more productive. An Institute grantee has identified characteristics which seem to predispose college men in later life to an increased incidence of old-age diabetes. These characteristics are high blood pressure, low lung capacity, overweight, and parents who had diabetes. Overweight seems to be the best predictor of subsequent diabetes. In another part of the study, characteristics apparently predisposing to coronary heart disease were identified, such as cigarette smoking, high blood pressure, physical inactivity, overweight, and early death of parents from coronary heart disease.

Advancing age is known to be accompanied by decline in the immune system—a system of specialized cells, organs, and body chemicals that protect from bacteria and viruses. The immune system may also protect from challenges within the body such as cancer cells. Scientists are investigatiing many aspects of immunity through studies with populations of aging mice and are beginning to pinpoint where in the system this wearing-out process begins. Their studies have shown that the major defect is the inability to produce enough cells capable of responding effectively to challenges. In their most recent work, these scientists have discovered that the inability of the immune system to operate effectively may be due to the presence of a certain type of white blood cell (a repressor) shown to be more common in old than in young mice. The investigators will now attempt to correct the defect in the immune system by removing the repressors. If this correction can be achieved, it could point the way toward beneficially modifying the immune system in the aged human.

An Institute-supported study has provided evidence that older persons suffer increased stress when forced into a new living situation. Investigators have shown that a group of older people who were forced to relocate because of urban renewal, increases in rent, or because their homes were condemned for health reasons, suffered increased morbidity and mortality. Examination of individuals anticipating relocation showed elevated blood pressure. Blood tests also indicated either a reduced food intake to the point of near starvation or exhaustion of the adrenal gland, an organ important in helping the body respond to stress. When compared with old people not facing relocation, the study group had far more hospitalizations for physical illness and psychiatric depressions, as well as a higher mortality rate.

The 1975 NICHD budget includes $13,855,000 for research on aging.

SUMMARY

In summary, Mr. Chairman, the budget request for the National Institute of Child Health and Human Development for 1975 totals $124,897,000.

I shall be pleased to try to answer any questions and supply additional information desired for the record.

CHILD HEALTH AND HUMAN DEVELOPMENT RESEARCH FACILITY

Mr. Flood. Dr. Corfman, in 1966 Congress appropriated $621,500 for planning a child health and human development research facility. Those plans ought to be ready by now. Have they been completed?

Dr. Corfman. They have been completed for several years.

Mr. Flood. Do you still need the facility?

Dr. CORFMAN. We very much need it. The facility is designated as building 33. It would provide for consolidation and efficiencies of operation of all of our intramural activities except those of the aging program housed in Baltimore.

Mr. FLOOD. Do you know why no funds for construction of the facility have been requested?

Dr. CORFMAN. I know they were requested in years past. I don't believe they were in the last 2 or 3 years.

Mr. FLOOD. Why not?

Dr. CORFMAN. I defer this to Dr. Stetten.

Dr. STETTEN. My understanding sir, and I have been in this job only 3 weeks, is that, in the priorities set within the Department and within the health agencies, these buildings have not attained sufficient importance to be requested.

Mr. FLOOD. There has been a realinement of priorities.

Dr. STETTEN. Yes; that is an appropriate phrase.

I know this building would be extremely useful, as Dr. Corfman has said. The present activities of his Institute are distributed among no less than 10 sites in and about Bethesda, in rented space, and in the handsome new building in Baltimore. Clearly a more effective operation will take place in a consolidated facility at Bethesda.

EMPLOYMENT

Mr. FLOOD. In fiscal year 1972 the Institute of Child Health and Human Development had 572 positions. In 1974 they were down to 521. What activities were curtailed as a result of this loss of 51 positions?

Dr. CORFMAN. I shall ask Mr. Hedetniemi to answer that.

Mr. FLOOD. And if you had new positions what would you do with them?

Dr. CORFMAN. I shall wait and answer that.

Mr. HEDETNIEMI. The reduction in positions has taken place across the Institute and has not resulted in a reduction of program activities but rather a consolidation of the staff who work on our respective functions. We have not eliminated programs because of these position cuts.

Mr. FLOOD. Point 2—new positions.

Dr. CORFMAN. The 10 new positions that have been requested are for the perinatal biology effort in the intramural program to permit staffing of the new facility now under construction at the clinical center.

SENILITY

Mr. FLOOD. Last year Dr. LaVeck told us the Institute was supporting almost no research at all on the problem of senility. Is that still the case?

Dr. CORFMAN. I am not sure of what you mean by senility.

Mr. FLOOD. Senility—period.

Dr. CORFMAN. We certainly have a major program in aging as you know. I don't know that we isolate senility as a special problem.

Mr. FLOOD. I am telling you what the man told us.

Dr. CORFMAN. My colleagues tell me that as defined in the context of these hearings we are not, in fact, doing any direct research on senility.

Mr. Flood. You are not. I thought that would be the answer. Don't you think the problem of senility deserves more attention?

Dr. Corfman. We have a major program in aging.

Mr. Flood. My question was don't you think that the problem of senility deserves more attention?

Dr. Corfman. Absolutely, but we are doing research related to senility and on the problems of older people.

Mr. Patten. Are you, Dr. Corfman?

Dr. Corfman. Yes, sir.

Mr. Patten. What do you mean you are filling in today?

Dr. Corfman. I am Acting Director today. The newly appointed Director is not onboard.

Mr. Flood. This Institute as of now has no Director.

Dr. Corfman. Dr. LaVeck left our Institute last year.

AGING RESEARCH

Mr. Flood. A lot of people believe that aging research will simply not get the attention it should as long as it is in the Institute run by gynecologists and pediatricians. Is there any merit to that argument?

Dr. Corfman. There are only two gynecologists in the Institute, and several pediatricians, but we do have gerontologists who are well known. Dr. Nathan Shock and his associates are internationally known. I would say the Institute does have gerontologists and that they are in charge of the aging program.

Mr. Flood. It is not an Institute run by gynecologists and pediatricians. Other people are onboard. Who is making the statement, you or me?

Dr. Corfman. As you know, the Directors of the Institute have been pediatricians, but the staff in charge of the aging programs are gerontologists.

ALLOCATIONS OF RESOURCES

Mr. Flood. How do you decide how much money and how much effort to allocate to, say, population research? There you have $45 million. Child health, $60 million. Aging, $13 million. How do you do that?

Dr. Corfman. It is a mix of factors that must be taken into consideration. One factor is the current program and another is the increment of change permitted by budget increases.

The third is evaluation of scientific need and the likelihood of making significant breakthroughs in an important area such as aging. These factors all have to be balanced. It is very difficult to launch an entirely new program when the increment is small.

AGING RESEARCH

Mr. Flood. Don't those figures indicate that research in aging has a very low priority? Don't they speak for themselves pretty eloquently?

Dr. Corfman. If one considers this only in the context that aging research is 12 percent of the Institute, it may seem so.

Mr. Flood. Perhaps? It is. Even you couldn't be more eloquent than those figures could you? You are not trying very hard but could you?

Dr. Corfman. The fact is $14 million is not an inconsequential amount of money to spend on a program.

Mr. **Flood**. That amount is not inconsequential even to the Appropriations Committee, but vis-a-vis the other figures that is important.

Dr. **Corfman**. There is a great deal of research related to aging going on in the categorical disease programs of other Institutes. When you add those research programs to our own the total is much greater.

POPULATION RESEARCH

Mr. **Flood**. Do you think we really need to continue to spend $45 million a year on population research with the birth rate declining?

Dr. **Corfman**. The question is close to home because that is my own field.

Mr. **Flood**. Well, come home. Go ahead.

Dr. **Corfman**. The answer is yes, absolutely. The mere fact that our birth rate has fallen doesn't mean population problems have been solved. For example, we certainly have a need for effective contraceptives that don't have serious medical effects. And we also need to know much more about the social science aspects of population problems.

It's just possible that in 5 or 10 years some will say that our population is getting too small. That was said in the midthirties. We need a research base on which to make judicious social judgments. Just because the birth rate is falling doesn't mean the population problem is gone.

Then I would say that NIH programs have an international significance. There are many countries where the birth rate is still dangerously high and our research will help these countries find solutions.

Mr. **Flood**. Recently we came across an announcement soliciting applications for research grants put out by your Institute that raised some questions in our minds.

I have here dated December 1973, Department of Health, Education, and Welfare, Public Health Service, National Institutes of Health:

"Dear Doctor." Apparently this went to everybody. The first paragraph I will quote.

> In answer to a considerable number of inquiries, this is to inform you that the Center for Population Research continues to be interested in research grant proposals on the behavioral-social science aspects of population, family planning, and reproductive behavior. This is viewed as a highly important long-term program with a need for more members of your discipline to become involved in population research. Research grant proposals submitted by social scientists in your profession will be carefully evaluated by expert reviewers for possible funding.

Signed by Dr. Sidney H. Newman.

We will put that in the record and the attachment.

[The information follows:]

Department of Health, Education, and Welfare,
Public Health Service,
National Institutes of Health,
Bethesda, Md., December 1973.

Dear Doctor: In answer to a considerable number of inquiries, this is to inform you that the Center for Population Research continues to be interested in research grant proposals on the behavioral-social science aspects of population, family planning, and reproductive behavior. This is viewed as a highly important long-term program, with a need for more members of your discipline to become involved in population research. Research grant proposals submitted by social scientists in your profession will be carefully evaluated by expert reviewers for possible funding.

Enclosed is an outline intended to give you some idea of the broad scope of population research areas appropriate to your discipline and of interest to the Center. This is meant to suggest research ideas, but you may think of additional ones, since the enclosure is not considered all inclusive.

The deadlines for submission of research grant proposals are February 1, June 1, and October 1. Proposals are submitted on appropriate forms which may be obtained from me.

It takes at least 6 months to process and evaluate the proposal. Investigators sponsored by profitmaking institutions are not eligible to submit research grant proposals.

I will be looking forward to hearing from you. If information is needed quickly, or if it is desired to discuss any matters with me, please call me (area code 301, 496-6515).

Sincerely yours,

Sidney H. Newman, Ph. D.,
Behavioral Science Administrator.

POLITICAL ASPECTS OF POPULATION, FAMILY PLANNING, AND REPRODUCTION RESEARCH

Research Problem Areas and Research Ideas

POPULATION AND REPRODUCTION GRANTS BRANCH, CENTER FOR POPULATION RESEARCH, NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT, BETHESDA, MD.

I. Population growth and size of population

A. Political implications of population size.

1. Effect of size of political unit on relationship between Government and citizen.

2. Effect of population size on political structures and legal processes.

3. Influence of population size on social conflict and political change.

4. Demand for public services as a consequence of differing levels of population size.

B. Political implications of population growth and change.

1. Effect of population change on political institutions and processes at international, National, State, and local levels.

2. Impact of differing rates of population growth on political and social institutions, on political demands, and on the allocation of Government resources.

3. Impact of population stabilization on political-social institutions.

4. The relationship between population change (including rate of change) and the cost and quality of various government services, such as schools, police protection, transportation, housing, et cetera.

5. The relation between population growth and change and political attitudes and participation.

6. Interaction between population growth and social policy: Impact of out-of-wedlock births, desertions, divorce, parental mortality, on public policies toward children and single-parent families; relationships between fertility rates, poverty, and public welfare policies; effect of social policies on reproductive behavior.

C. Influence of public and social policies and programs on population size, family size goals, the family formation process, fertility, mortality (especially infant mortality), and migration.

1. Pronatalist and antinatalist incentives and disincentives.

2. Laws and programs affecting the availability of contraception, abortion, and sterilization.

3. Laws affecting marriage, divorce, and illegitimacy.

4. Policies and programs affecting the status and role of women.

5. Policies and programs affecting children and child-rearing.

6. Tax structure.

7. National health, education, and social welfare policies and programs.

8. Immigration and emigration policies and laws.

D. Relation between political unrest, revolution, and wars, and fertility, mortality, and migration.

E. Elite perceptions of the relationship between population change and elite values; for example, economic growth, national power, national security; the impact of such perceptions on population policies, including pronatalist policies.

F. Relationship between rural population growth and legal systems: Analyses of the interaction between changing family size and inheritance laws, and impact on rural-urban migration; effects of population growth on size of land holdings and its impact on pressure for changes in land laws; for example, ceilings, legal relationships between tenants and proprietors, legal status of agricultural laborers.

II. Population composition

A political and social implications of population composition.

1. Relation of age structure to political attitudes and participation, and Government services; demand for Government services, such as child care programs, primary and secondary schools, housing, health programs, employment, social security; political decisions and budgetary priorities; status succession within the political system; level of innovation and propensity to change; political unrest and stability.

2. Relation of racial, religious, or ethnic composition of the population to the patterns of political participation; interest aggregation; demand for Government services; political decisions and budgetary priorities; composition of Government bureaucracy; political unrest and stability.

3. Relation of educational and income composition of the population to political participation; demand for Government services; impact of dependency ratio on the allocation of Government resources for social services; political decisions and budgetary priorities; interest aggregation; level of innovation and propensity to change; composition of Government bureaucracy; and political unrest and stability.

4. Relation of average family size to demand for and utilization of Government services, landholding, patterns of political participation, et cetera.

5. Analyses of the relationship between declining mortality and increased longevity on authority relationships within the family; effects of changes in family size and composition on the authority of parents and grandparents; population pressures within the family; impact of pressures on occupational choice and migration of the young adult; changing patterns of political socialization within the family.

6. Consequences of differential growth rates of racial, religious, and ethnic groups on the formation and implementation of public policies and programs.

7. Effects of differing rates of growth on sociodemographic distributions (age, income, and education) and their impact on the formation and implementation of public policies.

8. Interaction effects of racial, religious, and ethnic variables with educational and income variables.

B. Influence of public policies and programs on population composition.

1. Those applying to particular age, educational, or income groups.

2. Those which differentiate among racial, religious, or ethnic groups.

3. Immigration and emigration policies.

4. Policies and programs designed to affect population and family size; direct policies—for example, family planning; indirect policies—for example, day care centers, age of marriage laws, family allocation schemes, taxation; population responsive—for example, health and educational services; population influencing—for example, employment, housing construction.

III. Population distribution

A. Political implications of population distribution.

1. Relation of population distribution to political participation and other political factors; interest aggregation; demand for and utilization of Government services; political decisions and budgetary priorities; political unrest and stability.

2. Relation of changes in the urban-suburban-rural distribution to political institutions and processes; emigration as an alternative to political unrest; community organization of migrants to cities; socialization of farmers and peasants to urban life; interaction between migrants and the community to which they move; interaction between migrants and their place of origin; return migration and its political effects; migration nad new patterns of multiethnicity; elite response to migrants; political behavior of second-generation migrants.

3. Impact of density on political institutions and processes.

4. Effect of interregional and international migration on political institutions and processes.

B. Influence of public policies and programs on population distribution and concentration.

1. Those applying to housing, welfare, education, et cetera.

2. Those affecting the degree of consolidation or fragmentatiton of the structure of Government and public services.

3. Those which are aimed at the development or revitalization of economically depressed areas.

4. Those affecting particular economic sectors such as agriculture, industry, transportation, et cetera.

5. Impact studies : assessment of population distribution policies.

IV. Population policies and programs

A. Political factors and processes influencing the formulation and adoption of official population policies and family planning programs and the setting of program priorities.

1. Role of political parties, interest groups, private associations, and general public opinion.

a. Attitudes of groups such as planned parenthood associations, women's associations, the medical profession, demographers, economic planners, churches, universities, foundations, and racial and ethnic-based organizations.

b. Level of consensus and conflict within and among groups.

2. Role of external influences, for example, other countries and international organizations.

3. Attitudes and political ideology of Government leaders, bureaucrats, opinion leaders, and the public.

B. Political factors and processes influencing the communication, legitimization, and implementation of population policies and programs, such as family planning programs, population education programs, abortion and divorce legislation, et cetera.

1. Effect of different types of political systems ; analyses of conflicting values and goals within one or more systems.

2. Influence of political leadership and power structure ; intraelite conflicts on population policies.

3. Role and capacity of different Government agencies and levels of Government.

4. Function of political parties, interest groups, private associations, and public opinion.

5. Role of significant institutions, for example, church, schools, the press and other mass media, military and judiciary, et cetera.

C. Cross-national comparison of various countries' political and social characteristics in relation to adoption and implementation of population policies.

D. Impact of population policies and family planning programs on other elements of the political system and other social sectors ; consequences for economic growth, social conflict, political behavior.

V. Political aspects of population programs and research

A. Political implications of advances in reproduction, contraceptive technology, and genetics research.

B. Resource allocation for population policies, programs, and research ; relationship to other developmental goals and public policies ; utilization of research results as a basis for innovation and change in population policies and programs.

VI. Multidimensional research problem areas

A. Political implications of interaction among population size and composition variables, for example, for the form of Government, political participation, and demands on the political system.

B. Political implications of interaction among population size and distribution variables, for example, for political participation, administrative effectiveness, demand for and utilization of Government services, and national resources development.

C. Political implications of interaction among population distribution and composition variables, for example, for pattern of political participation, representation, power structure, Federal and non-Federal structures of Government, and demands for local or regional autonomy.

D. Relation between (A), (B), or (C) and capacity and willingness of various governments to adopt and implement an official population policy ; administrative responsiveness to the effects of Government programs ; feedback on administration.

E. Theories and methodologies linking demographic to political variables; the specification of intervening variables linking specific relationships.

1. Population density and interpersonal and group conflict and violence.
2. Population growth, political participation and demand-making behavior.
3. Relationship between age and political cognitions.

F. Policy evaluattion studies of population policies.

1. Relationship between policy and programatic outputs and client impacts.
2. Direct versus indirect policies.
3. Intended versus unintended effects.
4. Methodologies for assessing policy impacts, measuring effectiveness of alternative policies and programs.

Mr. Flood. Why should we go out and solicit grant proposals for this sort of thing when there are so many unfunded research budgets in almost every field of biomedical research? Why?

Dr. Corfman. Since we expect that our funding rate for competing approved projects in 1975 will be only 20 percent, I completely understand the dilemma you pose. The alternative to sending such a letter is not to stimulate scientists who we think are important to our field.

Mr. Flood. Do you have to go out and knock on doors?

Dr. Corfman. Dr. Newman does knock on some doors.

Mr. Flood. He did here. This is just "Dr. Blank." Every man for himself.

Dr. Corfman. That letter went primarily to sociologists and economists. Dr. Newman has done a splendid job in managing our grant program in the social sciences.

Mr. Flood. This went to all of the members of the social science association.

Dr. Corfman. Five years ago we had no population grants in the social sciences. Through the efforts of Dr. Newman and the rest of our group we programed a number of important grants, so many that the Division of Research Grants had to set up a new study section to review them. We knew at the time that these projects would compete in a tight funding situation, but we went ahead in a deliberate effort to involve scientists we think are important to our field.

INFANT MORTALITY

Mr. Flood. Of course I am pleased that the infant mortality rate in the United States seems to be declining. However, your justification notes that 13 other developed countries report more favorable rates.

Dr. Corfman. Right.

Mr. Flood. Why are we so far down the totem pole, so far down the listing?

Dr. Corfman. We have been for a long time.

Mr. Flood. I know that. That is another question.

Dr. Corfman. Whenever we get better they get better too.

Mr. Flood. That doesn't follow like night follows day by a long shot.

Dr. Corfman. The provisional infant mortality rate for 1973 was 17.6 for this country.

Mr. Flood. Why?

Dr. Corfman. Part of the reason is due to the way the statistics are gathered. If you would like, we would be happy to provide a more detailed analysis for the record. It is something that statisticians work and worry over a great deal.

Mr. FLOOD. So do we. That is hard to answer offhand but the question is as plain as the nose on your face. So the answer better be there. When this bill goes on the floor you will be sitting upstairs and Mr. Michel and I will be down in the well of the House under the gun. You can be sure somebody is going to inquire about this unless you have a pretty good answer in the record that will stop them when we tell them.

Dr. CORFMAN. It isn't just a statistical problem. It is a social problem as well. Most of the countries with lower rates are more homogeneous than ours, particularly the Scandinavian countries. They have few of the social problems seen in our central cities, and in our poor populations. Some people would say that we have a high rate because some Americans don't have access to proper medical care. If you would like a more detailed statement on this, we shall be pleased to provide it.

Mr. FLOOD. I should say. That is a hot one if there ever was one.

Place in the record the infant mortality rate for the United States compared with those other countries for the last 10 years.

Dr. CORFMAN. And an analysis of the reasons for our standing?

Mr. FLOOD. Yes, that will wake somebody up.

[The information follows:]

Testimony of
Dr. Philip A. Corfman

NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT
Infant Mortality Rates: Selected Countries, 1965-1971
(Rates are deaths under one year of age per 1,000 live births)

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Country	1971		1970		1969		1968		1967		1966		1965	
	Rank	Rate	Rank	Rate	Rank	Rate	Rank	Rate	Rank	Rate	Rank	Rate	Rank	Rate
Netherlands	1	11.1*	2	12.7	2	13.1*	2	13.4	3	14.7	2	14.4	2	14.4*
Sweden	2	11.7	3	13.1	1	12.9	1	12.9	1	12.6	1	13.3	1	12.4*
Finland	3	11.8*	1	12.5*	4	13.9	3	14.0*	2	14.2*	4	17.6	4	17.4*
Japan	4	12.4*	7	15.3*	5	15.3*	5	15.0*	11	19.3*	8	18.5*	5	18.5*
Norway	5	13.8	4	13.7	3	13.7	4	14.6	4	16.8	3	16.4	3	16.8*
France	NA		6	15.1*	8	16.4*	11	20.4*	6	17.1*	11	21.7*	11	22.0*
Denmark	6	14.2	5	14.8	6	15.8*	6	15.8*	5	16.9	9	18.7*	7	18.7*
Switzerland	7	15.1	8	15.4	7	16.1	7	17.5	7	17.8	6	17.8	8	19.0
New Zealand	8	16.7	9	16.7	9	16.9*	9	18.7	8	18.0	5	17.7	9	19.5
Australia	9	17.4*	10	17.9	10	17.8*	8	18.3	9	18.2	7	18.2	5	18.5
United Kingdom	10	18.0*	11	18.6	11	18.8*	10	18.8*	10	18.8*	10	19.6	10	19.6
Canada	11	18.8	13	19.3	15	20.8	14	22.0	14	23.1	14	23.6	15	24.7
German Democratic Rep.	11	18.8	16	20.0	12	20.4	11	20.4*	12	21.2*	12	23.2*	14	24.5*
United States	13	19.2*	14	19.8	14	20.7*	13	21.7*	13	22.1*	13	23.4*	15	24.7*
Ireland	14	19.6	12	19.2	13	20.6*	18	24.4	18	24.4	19	24.9	17	25.3*
Singapore	15	19.7	14	19.8*	15	20.8*	19	24.8	20	25.8	18	24.6*	NA	
Belgium	16	20.5*	17	21.7*	18	22.9	17	23.4*	16	23.7*	17	24.1	13	24.1*
Czechoslovakia	17	22.1*	18	22.9	18	22.9*	16	22.9*	16	23.7*	15	23.7*	17	25.3*
Israel	18	22.9	20	23.6	20	23.0*	21	25.9	19	25.3	NA		NA	
U.S.S.R.	18	22.9*	21	24.4*	22	26.4	NA		21	26.0	20	26.5	19	28.0
Federal Rep. of Germany	20	23.2*	19	23.5*	17	22.8	15	22.8	15	23.5	16	23.8*	12	23.8*

* Provisional at the time ranking was prepared.

NA - Not available.

Note: In 1967 the National Center for Health Statistics, using data from the 1965 Demographic Yearbook of the United Nations, established procedures and criteria for the ranking of countries by their infant mortality rates. Previously, problems had arisen because of the release of inconsistent data by various constituents of HEW and others. The criteria provide that the ranking be limited to sovereign countries with estimated populations of one million or more and with "complete" counts of live births and infant deaths, as indicated in the Yearbook. Data may not represent the same year for all countries, since the rate used is based on the latest data available for each country at the time the Yearbook goes to press.

Each year since the ranking of the 1965 data the NCHS has prepared rankings based on the current Demographic Yearbook. The rankings issued prior to 1965 were not developed according to the above criteria and are not comparable. We have checked with the National Center for Health Statistics for the 1972 ranking and have been informed they have not yet received the 1972 Yearbook.

National Institute of Child Health and Human Development

Testimony of
Dr. Philip A. Corfman

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ANALYSIS OF INFANT MORTALITY RATES

Following is an analysis of the rank of the United States in infant mortality rates for the past 10 years:

Although the United States ranks 13th in infant mortality, the United States has experienced a significant decline in infant mortality since 1965. Other countries such as Sweden, Norway, Finland, The Netherlands, Denmark, Japan, and Great Britain have also experienced a concommitant decline. Besides the relative homogenity of their populace, all of the countries with infant mortality rates lower than the United States, have national health delivery systems that insure that every pregnant woman receives medical care and supervision during pregnancy, labor, and delivery. The proportion of deliveries occuring in hospitals providing intensive care facilities for sick infants in Scandinavia is much greater than in the United States. Thus, because of better health system organization and service, fewer infants die in the countries with homogeneous, and centrally located populations.

The significant decreases in infant mortality rates beginning in 1965 have been most encouraging. A number of research and health service advances have contributed to the United States' significant downward trend. In 1965 the rate was 24.7 per 1,000 live births. Between 1965 and 1972, the average annual decrease was 3 1/2 percent in contrast to an average annual decrease of three-fourths of one percent between 1957 and 1965. It must be stressed that other developed countries have also witnessed this decline.

These significant advances made in research and delivery of health services can be attributed to the fields of obstetrics, neonatology, and the developmental sciences. For example, newer understanding regarding contraceptive control, pregnancy planning, general medical health of the expectant mother such as nutrition, preexisting disease, age, and parity has reduced reproductive failure and the number of infants born at high risk. Biochemical and biophysical monitoring techniques have given the clinician additional tools for evaluating fetal and maternal well-being. Fetal monitoring, urinary estriol, placental function studies, ultrasonography, and advances in treating concomitant maternal illness during pregnancy, labor, and delivery have insured an optimal environment in utero.

Separate, but equally important techniques, methodologies, and understanding of newborn illness have contributed to neonatal survival and well-being. Techniques of assessment of fetal disease by amniocentesis, pulmonary maturation in the fetus, and gestational age by electrophysiologic means have enabled babies previously born immature to be carried to term in many cases. New therapies for the neonatal respiratory distress have enhanced extrauterine adaptation. Basic scientific understanding of neonatal metabolic requirements has permitted advances in incubator design, infant transport, and chemical, thermal, and nutritional therapies for small babies. This latter understanding has made it possible to sustain infants and permit growth by the utilization of total parenteral nutrition. Immunological detection of infection and identification of causative agents, both congenital and acquired, have resulted from intensive efforts by basic scientists.

Few of these advances would have been possible without the recognition by medical specialists in obstetrics and neonatology that maternal and infant intensive care facilities were needed as well as highly skilled health care personnel. Within the past eight years significant advances in the organization and regionalization of maternal and infant health services in the United States have been made. This has enabled the high risk mother carrying the high risk fetus to obtain the highly specialized care necessary for optimal outcome. Concomitant with this effort has been the effort to develop and train health professionals, perinatologists, and nursing personnel mandatory to render these unique and specialized services to mothers and infants.

A high incidence of infant mortality represents a symptom of a society's social and health care system to provide for a heterogeneous population with divergent needs and inability to find or afford the services so vitally needed to maintain maternal and infant health. Infant mortality is a fundamental index of health in a population. It is not only significant as a problem in itself, but as an indication of factors related to more extensive and costly morbidity both medically and socially.

If an appreciable reduction in the United States infant mortality rate is to take place, attack upon the problem must include a multi-faceted, interdisciplinary approach which gives consideration to application of available knowledge, the identification of new knowledge and its early dissemination to related health professions and to the community at large, the provision and improvement of services to mother and child, the continuous evaluation of these services in order that deficiences might be identified and corrected early, and an increase in the manpower force to function in these areas.

During the first year of life the risk of dying is greater than during any other year until after age 65. Specific populations can be identified who are at greater risk in relation to a variety of variables. These include race, previous maternal health, parity, socioeconomic condition, and events in the perinatal period such as unexpected obstetrical emergencies.

Infant mortality is higher among the lower socio-economic groups for which health care services are less available and whose general health status is diminished. This includes the American Indian whose incidence is several fold greater than the White counterpart, and the Black population whose rate exceeds the white population by a factor of 1 1/2 to 2.

The greatest cause of newborn death is directly related to premature delivery and low birth weight infants. These infants require specialized services and care if they are to survive the first month of life. Within this first month of life, the period of highest mortality is the 24 hours prior to delivery and the first day of life. The infants at highest risk are those born prematurely with birth weights less than 5 1/2 lbs. Mothers under 16 and over 35 years of age, pregnant for the first time, of low socioeconomic status, and afflicted by certain diseases such as diabetes, heart, and kidney disease, have babies whose risk of dying is greater than if born of a healthy woman in her third decade of life. Infants less than 5 1/2 lbs. comprise only 8% of all livebirths but yield 70% of all neonatal mortality, of which over half is concentrated in the first 24 hours after birth.

Mr. PATTEN. Are you suggesting if you took the infant mortality rate, say, in some select county in Virginia you would find the figures would change?

Dr. CORFMAN. Yes. One finds that the Swedish-Americans in Minnesota about as well as Swedes in Stockholm. It is a social and economic problem too.

MENTAL RETARDATION

Mr. FLOOD. I have seen evidence of that, yes.

The birth rate is decreasing and the infant mortality rate is decreasing. Is there an increase or a decrease in the number of mentally retarded children who are born, and is there an increase or a decrease in the percentage of the children that are mentally retarded?

Dr. CORFMAN. It is very difficult to obtain firm figures on this issue. Nevertheless it is estimated that the numbers of mentally retarded children will decrease as we improve maternal and infant care and reduce the percentage of low birth weight infants. If these occur at a time when the birth rate is falling, the total number of mentally retarded infants will also probably decrease.

If I may go back to your earlier question on family planning, I would like to submit the calculation that if we were able to avoid all unwanted births the prematurity rate, the neonatal death rate, and the incidence of congenital malformations would all decrease significantly. Mongolism would decrease significantly also.

Mr. FLOOD. The lack of desire for the child will produce monoglism? The mere fact of desire?

Dr. CORFMAN. That is not what I meant. With the decrease in the birth rate, the number of unwanted children is going down. Our own data show that. This decrease means an improved infant mortality rate and a decrease in the number of mentally retarded children being born.

Mr. OBEY. Could I ask you to run that by me again? I don't understand why. Tell me why.

Dr. CORFMAN. You mean the significance of unwanted births?

Mr. OBEY. Yes.

Dr. CORFMAN. An unwanted birth is a birth that a woman or couple say at the time of an interview that they really didn't want.

Mr. CASEY. After the child is born?

Dr. CORFMAN. Yes.

Mr. OBEY. If those kids were not born, why would it result in the kind of statistics you just cited? Explain that to a layman.

Dr. CORFMAN. I think the best example is mongolism. As I said in the opening statement 50 percent of children with Down's syndrome are born of women over 35. We know from our studies that many babies born to women over 35 are unwanted. They say "I love that child but I really didn't want it. My husband and I weren't ready but we had it anyway."

If society were able to prevent the birth of all such unwanted children, the mongolism rate would go down because fewer women over 35 would have babies.

Mr. FLOOD. With a premise like that, Q.E.D.

Mr. Obey. Aren't you really talking about the number of babies who were born to women over 35? Wouldn't that result in a large percentage of the typical results you are talking about?

Dr. Corfman. It explains mongolism. As for prematurity, neonatal death and congenital malformations, these conditions have a high incidence in poorer women who are socially disadvantaged, especially very young women. Such women also have a high unwanted rate, since they don't have access to family planning services, they don't know where to go, and they don't have the money. If we were able to prevent births of unwanted children in these groups we would significantly reduce all these diseases.

Mr. Flood. You are asking for $18,639,000 for research on mental retardation. I don't have the figures at hand here but I do know we have been making substantial, and I mean substantial, amounts available for research on mental retardation for a number of years. Are we making any progress toward identifying the causes for mental retardation after all these years and all of this money?

Dr. Corfman. Yes. There has been a great deal of progress in 10 years, with 12 mental retardation centers as the prime focus of our research program. I think the Institute can point with pride to considerable advances.

One advance is the treatment of some of the causes of mental retardation.

Mr. Flood. I asked for the causes.

Dr. Corfman. One is PKU.

Mr. Flood. Translate.

Dr. Corfman. I refer to phenylketonuria. That and galactosemia are two diseases where treatment has been developed which considerably alleviates the diseases.

In our intramural program we are making progress, as I said in the opening statement.

Mr. Flood. Of course, Doctor, those are your two favorites. You mention those every year and then quit. Can you dust off a couple of others?

Dr. Corfman. Let me review the causes.

Mr. Flood. That is what I asked you.

Dr. Corfman. We have mentioned in the past the work on hemophilus influenza vaccine. We tend to repeat reference to such work because it will have a significant impact.

Malnutrition is an issue of great interest in many parts of our Institute. We now have a much better understanding about the relationships between the nutrition of mothers and their children, especially mothers during pregnancy and lactation.

Mr. Flood. Were you making the statement that malnutrition was causing mental retardation?

Dr. Corfman. There seems to be some evidence that malnutrition contributes to retarded mental development, particularly when malnutrition occurs during pregnancy and early childhood. The findings arising from the Guatemala study and other coordinated studies supported by NICHD are sharpening our knowledge of the nature and timing of this retardation, as well as possible ways to intervene so as to prevent it.

GENETIC AND ENVIRONMENTAL FACTORS

Mr. **Flood.** This is another one that has been around. Do we know, for example, to what extent this is caused by genetic factors, to what extent by environmental factors?

Dr. **Corfman.** We say that 2 percent of mental retardation is genetically determined and 5 percent has a mixture of causes. This mixture of conditions includes infectious diseases which mimic genetic diseases, such as German measles, certain fungus diseases, and syphilis.

Mr. **Flood.** After all of that, are there any promising proposals for research on mental retardation which might be approved if we made additional fundings? That is a leading question.

Dr. **Corfman.** I shall be glad to provide that information for the record.

[The information follows:]

National Institute of Child Health and Human Development

REQUIREMENTS FOR ADDITIONAL FUNDING IN MENTAL RETARDATION

Following is a description of research in mental retardation which would be undertaken with additional funding:

Infancy through the first 5 years of life is a period when the central nervous system is most modifiable as a consequence of experience. This period, therefore, presents distinct opportunities for a wide variety of psychological and educational interventions designed to optimize the development of infants and young children showing early signs of aberrant development including developmental delay. The opportunities and research leads in this area are, today, largely unexploited. A stronger effort here would carry the promise of bringing more of these high-risk infants to school age with increased capability for adapting more fully to school and community life and with less demand for special community resources. With greater research capability, the Institute would move to support more research on early diagnosis concerned with early specification and identification of risk infants so that they could be placed in intervention programs most profitably; develop methods and materials to assist parents in the care and training of their risk infants (parents have been shown to use these effectively); and develop the basic science undergirding sound intervention efforts.

National emphasis, today, is being placed on assisting retarded individuals to avoid life in institutions by encouraging ther adaptaton, to, and partcipation in their local communities. Research leads suggest that intermediate care facilities can be helpful, but the methodologies for their services are weak. Research on the problems concerned with effective training in intermediate care facilities needs to be undertaken and would be fostered.

The movement of the retarded from institutions to their home communities is being accomplished without adequate safeguards for measuring the effects of these changes on the retarded, the community problems they face, and the problems this presents to communities. Dispersal of the retarded population into our communities make their problems and conditions of care less obvious. Research studies to investigate these conditions are needed and would be pursued.

Mr. **Flood.** Do you think that much of the mental retardation which now occurs is preventable if we had proper prenatal and postnatal care of the mother and the baby?

Dr. **Corfman.** It should have a significant impact. I was about to continue in my review of the things we have done in mental retardation research and to say that one of our important activities involves people who are socially disadvantaged. Seventy-five percent of mental retardation is classified as mild. Many of those children improve tremendously with relatively simple but careful treatment and care. We have made great progress in that area.

Mr. Flood. You touched upon this. Of course you would and so would we. What kind of research leads, actual research leads, are being pursued with respect to sudden infant death syndrome? What leads do we have and are they just hanging in the air or are we pursuing them?

Dr. Corfman. Would you like a relatively detailed analysis of that for the record?

Mr. Flood. Yes.

[The information follows:]

National Institute of Child Health and Human Development

THE SUDDEN INFANT DEATH SYNDROME

In the United States, the sudden infant death syndrome (SIDS), also known as crib death, is the leading cause of death among infants between the first and twelfth months of life. It is estimated that about three infants per 1,000 live births succumb to this syndrome. Most victims are between the ages of one and six months. The frequency is highest between the second and fourth months of life.

The National Institute of Child Health and Human Development (NICHD) of the National Institutes of Health has primary Federal responsibility for research on the sudden infant death syndrome. Other Federal programs related to SIDS involve the National Institute of Neurological Diseases and Stroke (NINDS) of the National Institutes of Health, the National Center for Health Statistics of the Health Resources Administration, and the Bureau of Community Health Services, Maternal and Child Health of the Health Services Administration.

Obligations for programs in Sudden Infant Death Syndrome

	1971	1972	1973	1974 estimate	1975 estimate
National Institutes of Health:					
National Institute of Child Health and Human Development......	$1,800,000	$3,550,000	$4,106,000	$4,700,000 *($5,000,000)	$4,700,000
Health Resources Administration:					
National Center for Health Statistics......	---	---	11,000	---	---
Health Services Administration:					
Bureau of Community Health Services:					
Maternal and Child Health................	---	35,000	---	---	---
Total...............	1,800,000	3,585,000	4,117,000	4,700,000	4,700,000

*1974 figures in parentheses represents 1974 base figures plus 1973 restoration.

NATIONAL INSTITUTES OF HEALTH

National Institute of Child Health and Human Development

Crib death strikes without warning. In the majority of cases the baby is apparently in good health and feeds without difficulty. While there may be evidence of a slight cold or stuffy nose, there is no history of serious upper respiratory infection. The infant is placed in his or her crib for a nap or for the night and several hours later is found dead. Following autopsy, no cause of death can be identified.

The sudden infant death syndrome (SIDS) is a world-wide health problem. It occurs more frequently in males than in females, in non-white than in white babies, in families of lower socioeconomic status, in premature infants, particularly those who had gestational ages between 34 and 35 weeks, and in babies who had recent infections. Twins may be especially vulnerable to SIDS. It is likely that this tendency is related to their typical lower birth weight or shortened gestational period.

Most crib deaths in the United States occur in the cold weather between November and March. Sudden changes in temperature may trigger the syndrome. The risk appears to be highest in crowded environments. Autopsies show a high incidence of minute hemorrhages within the chest in victims who are otherwise free of abnormal tissue changes. This may be due to a short, but silent, terminal struggle to breathe.

Why these babies die is unknown. Many reasons have been offered to explain the deaths, including neurophysiologic, immunologic, cardiorespiratory, endocrine, and infectious disease causes. None to date has explained it correctly. All factors believed to be associated with the syndrome appear to be intertwined. It is not known, however, which one of the associations is most important.

Research Objectives in SIDS

Beginning in April 1971, NICHD intensified its research on the sudden infant death syndrome. The objectives of this expanded effort are:

1. To increase understanding of underlying mechanisms of the syndrome.
2. To discover its probable cause or causes.
3. To identify infants at risk of becoming victims.
4. To explore preventive approaches.
5. To stimulate scientists to direct investigative efforts toward solution of this complex problem.
6. To elucidate the impact of a sudden and unexpected infant death on the subsequent behavior of parents, siblings and the extended family.

7. To learn more about the management of SIDS cases in the United States and to develop guidelines for coroners, medical examiners, and pathologists in handling these cases.

8. To provide training of scientists with interests in neurophysiology, cardio-respiratory physiology, metabolic and thermoregulatory processes, epidemiology, pathology, immunology, infectious disease and social psychology related to the syndrome.

9. To support interdisciplinary conferences and workshops.

10. To prepare and distribute scientific publications and public information materials.

Seven Emphasis Areas in SIDS Research

The NICHD has developed its SIDS research around seven emphasis areas:

1. Abnormal sleep patterns related to breathing and circulation and other functions essential to life.

2. Respiratory, cardiac, and circulatory responses to such stimuli as excess carbon dioxide in the blood or oxygen deficiency, which may make some babies likely to die.

3. The body's system for temperature regulation and its response to environmental conditions existing at the time of death.

4. The baby's developing immune system and how defects in development may predispose an infant to the syndrome.

5. The distribution of the sudden infant death syndrome within the population and characteristics surrounding its occurrence in order to identify infants at high risk and to determine its causes.

6. Studies of the structural and functional changes in tissues and organs which may be involved.

7. The psychological stresses experienced by the family and the community when a sudden and unexplained infant death occurs.

The NICHD has sponsored a series of planning workshops to consider the nature and scope of this problem, identify new approaches, and highlight specific research questions in need of in-depth study. These workshops bring together investigators with expertise in areas having direct relation to the syndrome. The workshops have been beneficial in expanding the horizons of knowledge and have attracted qualified scientists to work on the problem of SIDS. Four workshops were held in 1972, four in 1973, and three planned for 1974. A summary report of each workshop is published.

Specific Research Projects

In FY 1973 the NICHD provided support for 72 research projects aimed at understanding the syndrome. This included 11 grants and contracts specifically concerned with SIDS and 61 for pertinent related studies. FY 1973 support approximated $4.1 million compared with $3.5 million in FY 1972. Funding for FY 1974 is estimated at approximately $4.7 million.

The Institute's expanded research on the syndrome and staff consultations have stimulated numerous inquiries and grant applications. In FY 1973, 21 grant applications directly related to SIDS were reviewed by the National Advisory Child Health and Human Development Council. Seven were recommended for approval; five have been funded. Institute staff members have communicated with all applicants whose proposals were not approved or will not be funded, in an effort to help them improve their applications.

In several of the workshops, the importance of finding animal models suitable for research was stressed and deemed essential to an understanding of underlying mechanisms. To implement this recommendation, the Institute solicited proposals and negotiated two contracts aimed at developing animal model systems for research.

Contract Studies

One contract calls for a broad approach including the relationship of genetics, infectious disease, immunologic and epidemiologic factors to onset of naturally occurring sudden and unexplained death in kittens. The other contract involves study of how the larynx and its nervous control may relate to the arrest of breathing in fetal and newborn lambs and kittens. The investigators are particularly concerned with effects of fluids such as water (with and and without sugar) and milk on closure of the upper airway.

In June 1972, the Institute contracted with Children's Orthopedic Hospital in Seattle, Washington to survey current management of sudden infant death cases in a sample of standard metropolitan statistical areas in the United States.

Among the findings from this survey are that: 1) there was a considerable lack of knowledge about crib death among public health and safety officials, which often resulted in a lack of sensitivity to the needs of bereaved parents; 2) there was a positive correlation between knowledge about crib death on the part of officials involved in SIDS and the degree of supportive management demonstrated in the handling of these cases; 3) poorer people were more likely to be handled with a lack of understanding than others; and, 4) some medical examiners had been quite sensitive to the needs of bereaved parents so that the impact of SIDS deaths was lessened.

The results have emphasized need for broad distribution of information about crib death to medical examiners, public safety officials, hospital emergency room personnel, pediatricians, nursing personnel, and parents. The Institute is now preparing a document to achieve this, which will be available during FY 1974.

New Leads

New leads evolving from NICHD-supported activities include:

1. SIDS May be Related to Heart Rate Changes, Apnea, and Infection. All infants demonstrate breathing irregularities during their normal sleep. A scientist at the State University of New York at Syracuse showed that some infants have prolonged halts in breathing (apnea) during transition into rapid eye movement (REM) sleep--a particular period of "active" sleep which normally occurs several times during a sleep cycle. Furthermore, this investigator found a relationship between apnea episodes and changes in heart rate, and that infections in the upper airways appear to increase the sleep-related episodes of prolonged apnea and associated slowing of heart rate.

2. SIDS May be Related to Lack of Sleep. An investigator at the School of Medicine of the University of California at Los Angeles is studying the relationship of these temporary halts of breathing to patterns of sleep in kittens. An important observation is his finding that the frequency of apnea was greatly increased following prolonged periods of lack of sleep. The ability of a kitten to wake itself during a period of apnea was also reduced during REM sleep and following sleep deprivation. Moreover, spontaneous spasms in the larynx were frequent during REM sleep.

These observations are important because a prolonged apneic period occurring at a time when arousal mechanisms are suppressed could lead to a lack of oxygen in the tissues and central nervous system depression. Such depression could result in sudden death without pathologic findings. It is also possible that a laryngeal spasm occurring at a time when waking up mechanisms are depressed , could precipitate death.

3. SIDS Babies May Lack Oxygen. Another investigator, at the Hershey Medical Center of Pennsylvania State University, has demonstrated enlargement and abnormal growth of smooth muscle fibers in small arteries of the lung area of babies who had died from SIDS. The findings suggest that these infants experienced long-term lack of oxygen in the lung, since such an increase is known to be associated with oxygen lack.

4. SIDS May be Related to an Abnormality in the Brain Stem. A scientist at the Montefiore Hospital and Medical Center, New York, has proposed that an abnormality in a part of the lower brain stem which is involved in control of normal breathing may cause disruption of the breathing cycle, leading to apnea during sleep. Investigators propose to test this hypothesis by studying breathing patterns and electroencephalograms (EEG's), in a group of SIDS "near misses"--infants who stopped breathing and required resuscitative efforts for survival. These babies are thought to be potential victims of the sudden infant death syndrome.

5. SIDS May be Related to Immaturity of the Nervous Mechanism Controlling Heart Function. A group of scientists at University of Southern California believe that there may be a relationship between SIDS and immaturity of the mechanisms controlling heart function. They have found by looking at records of babies who later died of SIDS that the babies had a tendency toward high levels of carbon dioxide in their systems and certain abnormalities in heart function during and just after delivery. These studies suggest that immaturity of the nervous system controlling the heart might be identified by monitoring fetal heart rate during labor.

6. SIDS May be Associated With Obstruction Due to Viruses in the Blood Supply of Lung Area. A pathologist at the University of Tennessee, using several methods, will look for evidence of viruses at autopsy of SIDS victims. He will also determine the concentration of oxygen in the blood in the left side of the heart (left ventricle) in order to ascertain whether the babies died primarily from respiratory failure. Individuals with pulmonary death tend to have low oxygen concentrations in the left side for many hours after death while patients who die from other causes have higher oxygen levels in the left side.

7. SIDS May Result from Inadequate Lung Responses. A scientist at the Hospital for Sick Children in Toronto, Canada will study the hypothesis that some infants' lungs cannot respond to stress on their respiratory system and that this might contribute to the occurrence of SIDS.

NICHD Information Program

The National Institute of Child Health and Human Development is continually expanding the availability of publications for distribution to the scientific and lay communities as part of its sudden infant death syndrome information program. Publications currently in print include:

Summary of Proceedings: Second International Conference on Causes of Sudden Infant Death Syndrome, Seattle, 1969

SIDS: Selected Annotated Bibliography, 1960-1971

Research Planning Workshop on The Sudden Infant Death Syndrome

SIDS Research Planning Workshop: Developmental Aspects of Infection and Immunology

SIDS Research Planning Workshop: Neurophysiological Factors

Facts About Sudden Infant Death Syndrome

Publications currently in preparation for distribution in FY 1974 include:

SIDS: A Family Crisis

SIDS: Information for Parents and Rescue Workers

SIDS: Management of Cases in the United States

SIDS Research Planning Workshop: Cardiorespiratory Phenomena

SIDS Research Planning Workshop: Behavioral Considerations

SIDS Research Planning Workshop: Epidemiology

SIDS Research Planning Workshop: Pathology

The NICHD has convened an HEW Interdepartmental Committee on Federal Efforts in the Sudden Infant Death Syndrome. This group meets quarterly to discuss SIDS activities of each program and progress being made by each group. The Committee was established to enhance communication, to keep all involved groups informed of ongoing Federal activities in SIDS, and to identify new approaches as warranted.

In addition to NICHD staff, there is representation from NINDS, NIMH, Bureau of Community Health Services, Health Services Administration, and the National Center for Health Statistics, Health Resources Administration. Plans are under way to include representation from other related and interested federal programs.

HEALTH RESOURCES ADMINISTRATION

National Center for Health Statistics

The Health Resources Administration (HRA), National Center for Health Statistics, is also supporting some work in SIDS. As a result of work with the World Health Organization, the coding of SIDS deaths has changed beginning with the 1973 data year. Now all SIDS deaths will receive the same ICDA (International Classification of Diseases Adapted), code (795.0), whereas previously they had been coded to four different categories along with non-SIDS deaths.

In addition, all mention of SIDS will now be coded, even those occurrences which have specific diseases mentioned along with them. This will enable more accurate counts to be made of the number of death certificates which mention SIDS, thus greatly facilitating research on SIDS.

NATIONAL INSTITUTES OF HEALTH

The National Institute of Neurological Diseases and Stroke

Because of valuable data already available, the National Institute of Neurological Diseases and Stroke (NINDS) has negotiated a contract related to SIDS with the University of Pennsylvania. The Collaborative Study on Cerebral Palsy, Mental Retardation and Other Neurological Diseases of Infancy and Childhood, a prospective study which has monitored events, conditions and abnormalities of 50,000 women during their pregnancies, included an analysis of an estimated 75-100 cases of the sudden infant death syndrome. The contracting university will assess the data on the women, their pregnancies, and their offspring who became victims of SIDS, and compare them with a set of matched controls.

HEALTH SERVICES ADMINISTRATION

Bureau of Community Health Services, Maternal and Child Health

The principal activities of Maternal and Child Health (MCH) in the sudden infant death syndrome have been to produce a training film and to conduct a series of regional conferences for professional and community health workers.

The training film, "One in Three Hundred and Fifty" was produced with a $30,000 MCH grant made to Dr. Abraham Bergman at Children's Orthopedic Hospital in Seattle, Washington. This 16mm. black and white 25-minute film is a documentary in which four sets of parents discuss their experiences following a sudden and unexplained infant death. The purpose is to introduce an awareness of the problem of SIDS and to learn more effective ways to assist families following such a loss. Four copies of this film will soon be available on a rental basis through the Foundation for Sudden Infant Death, New York City.

Children's Orthopedic Hospital in Seattle was awarded a second grant of $9,800 for a series of regional conferences on the sudden infant death syndrome, to run from July 1, 1972 through June 30, 1974. Eleven conferences are planned for this period.

The largest group of participants at conferences were nurses employed in public health, pediatrics, and emergency services. State and regional consultants in maternal and child health participated in large numbers. Physicians, social workers, clergymen, lawyers, psychologists, law enforcement officers, coroners and medical examiners have also attended.

A typical conference includes opening sessions during which participants learn about the incidence and origins of the syndrome. Discussion by a panel of parents who have experienced a loss or showing of the movie "One in Three Hundred and Fifty" precede consideration of the psychological impact of such an event and its aftermath. The second segment of the program is a discussion of specific topics with participants in smaller groups. Qualified group leaders and participants discuss the impact of a sudden infant death on siblings and relatives, distinctions between SIDS and child abuse, the process of grief and mourning, "red tape" following such a death, the need for parental support and counseling, assistance to parents after the birth of subsequent children, and organization of community agencies to provide necessary services to parents following the loss of an infant. The conferences generally close with consideration of future research, education and services that are needed.

The effect of these conferences, plus the continued distribution of teaching materials through the regional MCH program staff to the MCH staffs in State Departments of Health, MCH Special Projects and institutions of higher learning, is becoming more evident. In some states such as Arizona, MCH formula funds are being used to support statewide services. Nursing consultants in the State Department of Health of Colorado have been providing direct counseling and follow-up to parents in remote areas.

In Montana, the state MCH staff conducted a two-part SIDS in-service (March and June 1973) for public health and hospital nurses. The Kansas State Health Department nurses had a similar in-services program for clinical specialists counseling families in well-child conferences, family planning settings and MCH projects. At a meeting of MCH nursing consultants and clinical specialists, in Denver, a paper on SIDS was presented to stimulate interest and encourage participation in local area programs

It should also be noted that there is greater inclusion of material on SIDS in university programs. The syndrome has been presented in "pediatric grand rounds" at the University of Colorado and in Boston. Nursing schools are finding more student interest expressed in this syndrome. In addition, SIDS has become a part of the study of the broader area of death, grief and mourning of parents who lose an infant or child from any condition.

Mr. **Flood.** Are we any closer to solution of this mysterious syndrome?

Dr. **Corfman.** We know a lot more about it than we did several years ago when the Institute began its program.

PROJECT CONTRACTS

Mr. **Flood.** There is $20,218,000 in your budget for research and development contracts. What kind of research do you support under contracts? Give me a couple of examples of that.

Dr. **Corfman.** Examples of the substance, or the strategy?

Mr. **Flood.** You have contracts. What kind of research do you support under a contract?

Dr. **Corfman.** Most of our contracts are in population research. We use contracts for our drug development, for the synthesis of new compounds for their testing, for the development of new sterilization techniques for men and women.

We also have a number of contracts on evaluating the medical effects of contraceptives in use. Contracts are also used to fund portions of our research programs in child health and aging.

Mr. **Flood.** When you get this record and take a look at it don't think you are handcuffed by what you said here. When you look at it, if and when you feel this record should be embellished or developed please do it. Don't hestitate to do that. Some people don't know but you do, don't you?

Dr. **Corfman.** I was beginning to review all of our contract programs.

Mr. **Flood.** Do that for the record as you see fit.

Dr. **Corfman.** Provide a description of our total contract program?

Mr. **Flood.** Whatever you want to say, yes.

[The information follows:]

NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT

Description of National Institute of Child Health and Human Development's Contracts Program

The contract mechanism provides the Institute with an effective instrument for supporting direct research which has been determined by Institute staff to be of high priority and over which the Institute requires greater control of timing and methodology than would be the case under grant supported research. Contract research is carried out in educational institutions, nonprofit organizations, and industrial concerns. This mechanism is a complement to the Institute's programs carried on directly in Government laboratories and those supported through research grants.

Population research and development contracts cover the fields of: contraceptive development; evaluating the medical effects of existing contraceptives; and social science research. Respective examples of contract efforts include: the development of implantable contraceptive devices for the male; interaction of contraceptive steroids with vitamin E; and the role and fertility patterns of urban mothers.

Each of the three major components of the child health research program utilizes research and development contracts. The perinatal biology and infant mortality program has given increased emphasis to the sudden infant death syndrome while continuing prenatal, maternal, and infant health research. Mental retardation research programing has recently emphasized the prevention of prematurity and developmental mental disorders, diagnostic and intervention studies of high-risk infants, a behavioral phenotype in the cornelia delange syndrome, and amniocentesis evaluation. The recent emphasis in the growth and development program concentrates on the study of the normal growth processes, the effects of malnutrition on children, and adolescent development.

Much of the research and development contract effort in aging continues to provide for development of vital resources needed by investigators in the field. One of the most important resources to investigators is a supply of animals partciularly suitable for aging research. Studies are also being conducted to obtain a better understanding of the biological, including immunological, and psychological bases of the aging process.

Mr. Flood. Who are some of the larger contractors?

Dr. Corfman. The largest contract in the population field is the one with Kaiser Permanente in California, which is doing a long-term study of oral contraceptives. We can provide more detailed information.

Mr. Flood. Do this: Give us a list of the 10 largest contractors in fiscal year 1974 with a description of the work and of course the amount of dollars that are involved.

Dr. Corfman. Yes, sir.

[The information follows:]

NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT

NICHD's Ten Largest Contractors - 1974

Following is a list of the ten largest contractors funded for the first six months of fiscal year 1974. Estimates for the entire fiscal year 1974 cannot be completed at this time because of the competitive nature of research and development contract bidding. Therefore, in addition, a list of the ten largest contractors in fiscal year 1973 is also included.

CONTRACTOR	LOCATION	CONTRACT NUMBER	TITLE	AWARD PERIOD	AMOUNT
1. Kaiser Fn.Hosp.	Oakland, Ca.	NO1-HD-3-2710	Contraceptive Drug Study	12/1/73-11/30/74	
			Description: Obtain longitudinal clinical and biochemical information on 17,000 women of reproductive age with reference to their use of contraceptive methods. Emphasis is on longitudinal surveillance of inpatient and outpatient data as determined from a retrospective examination of already available records for these women, prospective surveillance of inpatient and outpatient records, and annual medical examinations through an automatic multi-phase laboratory.		$766,401
2. Illinois Inst. of Technology	Chicago, Ill.	NO1-HD-1-2229	Design and development of Implantable Contraceptive Devices for the Male	9/30/73-9/29/74	$200,694
			Description: Development of a vasectomy device made of flexible medical-grade silicone which will produce aspermia when implanted in the "off" position and will allow transport of viable sperm when reversed to "on" position.		
		NO1-HD-1-2233	Intra-Uterine Sterilization System for the Female	9/30/73-4/29/74	483,769
			Description: Development and testing of a clinical prototype steerable hysteroscope which permits the direct transcervial observation of the interior of the uterus including the openings of the oviducts into the uterus. The instrument offers the potential for the nonsurgical placement of occlusive devises into oviductal openings for sterilization purposes.		$684,463
3. Columbia University	New York, N.Y.	NO1-HD-2-2038	Role and Fertility Patterns of Urban Mothers	8/1/73-6/30/74	$ 59,394
			Description: Investigating and analyzing data gathered by survey on the relationship between female roles and fertility, focusing on the time of the first birth as an intermediate variable.		
		NO1-HD-9-2180	Prevention of Prematurity and Developmental Disorders	10/1/73-9/30/74	568,514
			Description: Exploring the effectiveness of prenatal care in the prevention of prematurity and developmental disorders through nutrition protein supplement to the ordinary diet in categories of pregnant women at high risk of producing premature babies.		$627,908

CONTRACTOR	LOCATION	CONTRACT NUMBER	TITLE	AWARD PERIOD	AMOUNT
4. Univ. of North Carolina	Chapel Hill, N.C.	N01-HD-4-2804	Consequences of a Reproduction Model; A Utility of Reproductive Behavior	11/1/73-10/31/76	
			Description: Testing a utility model designed to predict the probability of various reproductive events of couples in the light of their expectations and perceptions of the consequences of reproduction. This will be aided by the development, administration and analysis of a survey of a sub-sample of 1200-1500 women under age 30 and married.		$455,648
5. Temple University	Phila.,Pa.	N01-HD-1-2299	Study of Cervical Cytology in Contraceptive Users	10/1/73-9/30/74	
			Description: Studying the Relationship between oral contraceptive pill usage and abnormal cervical cytology. He has developed a cohort 21,500 women whom he has been following longtitudial basis. During the current year the contractor will complete data analysis and prepare his final report.		$392,215
6. Univ. of California	Los Angeles, Ca.	N01-HD-1-2215	A Study of the Growth of Mexican-American Families	12/1/73-5/29/74	$ 23,176
			Description: Studying the determinants of fertility and family planning among Mexican-Americans in Los Angeles County. This includes design, administering and analysis of a survey.		
		N01-HD-2-2701	The Employed Woman: Family Planning and Career	10/1/73-6/30/74	34,820
			Description: Researching the attitudes, motivations and practices of married professional career women related to fertility and family planning. This includes the administration and analysis of a survey.		
		N01-HD-2-2778	Developmental Phenomena and the Occurrence of SIDS	10/1/73-10/31/73	15,000
			Description: Continuous 12 hour polygraphic recording of EC,EOG,EMC impedence pnerimograph.		
		N01-HD-4-2810	Developmental Phenomena and The Occurrence of SIDS	11/1/73-9/30/74	234,300
			Description: Performing data analysis on 12 hour recordings of human infants who have been divided into two subgroups (high risk for SIDS and low risk for SIDS). Studies are also being undertaken in newborn cats to determine if you can experimentally induce a spontaneous reaction which reults in sudden death. This data is also analyzed under this contract.		$ 307,296

CONTRACTOR	LOCATION	CONTRACT NUMBER	TITLE	AWARD PERIOD	AMOUNT
7. Princeton Univ.	Princeton, N.J.	NO1-HD-0-2077	An Analysis of the Decline of Fertility in Europe	11/1/73-10/31/74	$ 49,603
			Description: Studying the decline of fertility in Europe by using four indices of fertility and nuptiality computed for over 700 provinces in Europe at 10-year intervals. The indices measure (1) overall fertility; (2) Marital fertility, (3) proportion married among women of childbearing age, and (4) the fertility of unmarried women.		
		NO1-HD-1-2138	Support of Publication of Population Index	9/25/73-9/24/74	90,879
			Description: Preparing bibliography for publication in the Population Index to include selection of significant works, preparation of bibliographical citation, translation, annotation and integration of citations into a conceptual scheme of demography.		
		NO1-HD-5-1048	Survey of Fertility and Contraceptive Practices	10/1/73-9/30/74	165,699
			Description: Continuing the National Fertility Study by tabulating and analyzing 1970 data, completing the report of the 1970 National Fertility Study and continuing to maintain a current address file.		$ 306,181
8. Resources for the Future, Inc	Wash., D.C.	NO1-HD-4-2805	Economic and Environmental Consequences of Population Change	12/15/73-6/14/75	
			Description: Studying the economic and environmental effects of population change by refining existing models to provide estimates of the effects.		$ 283,126
9. U.S. Dept of Commerce, Bur. Census	Wash., D.C.	YO1 31012 01	Child-Spacing and Current Fertility: 1970 Census	7/1/73-6/30/74	
			Description: Collecting, tabulating, researching and analyzing data by social and economic characteristics for diverse population groups on (1) age at marriage and birth intervals, (2) the effect on fertility of separation and of marital dissolution and remarriage, (3) unintended childbearing, and (4) social and work roles.		$250,000

CONTRACTOR	LOCATION	CONTRACT NUMBER	TITLE	AWARD PERIOD	AMOUNT
10. Univ. of Missouri	Columbus,Mo.	NO1-HD-2-2769	Evaluation of a Reversible Vasectomy Prosthesis	9/30/73-9/29/74	$ 25,000
			Description: Analysis of a reversible vasectomy prosthesis made of silastic tubing and studies of its effect on reproductive tissues and function.		
		NO1-HD-2-2772	Immunologic and Morphologic Consequences of Vasectomy	10/1/73-9/30/75	203,750
			Description: Studying the morphological and functional changes after vasectomy, the role of the immune response in the development of these changes, and the role of antibody in protecting against immunologically mediated damage. This study is being performed in guinea pigs and will tell what effect vasectomy has on the body's immune response mechanism.		$228,750

NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT

NICHD's Ten Largest Contractors - 1973

CONTRACTOR	LOCATION	CONTRACT NUMBER	TITLE	AWARD PERIOD	AMOUNT
1. Temple University	Philadelphia, Pennsylvania	NO1-HD-1-2142	A Study of Physicians Attitudes Toward Abortion	12/15/72-7/14/72	$44,000
			Description: Investigating physicians' attitudes toward, knowledge of, and behavior concernin— abortion. This includes constructing, administering and analyzing an interview schedule.		
		NO1-HD-1-2299	Study of Cervical Cytology in Contraceptive Users	10/22/72-10/31/73	1,539,644
			Description: Define a cohort for a prospective study of cervical cytology among contraceptive users. A total population of 35,000 patients shall be enrolled. The objective of the study is to observe changes in cervical cytology as related to contraceptive use over a period of at least 5 years.		
		NO1-HD-3-2723	Fertility-Related Decision-Making Among Married Couples	6/15/73-6/14/74	120,369
			Description; Investigating the nature and etiology of decision-making and implementation processes related to fertility regulation by married couples. This will be done by administration of an University of California interview to a probability sample of 450 married couples living in metropolitan, suburban and rural areas.		
		NO1-HD-3-2749	Novel Steroids With Potential Antifertility Activity	4/24/73-4/23/74	26,990
			Description: Procure 100 to 500 milligram quantities of compounds involving novel sprio steroids, cyclopropyl steroids and ring A bicyclo [3,2.0] heptanes for investigation as potential antifertility agents.		
					$1,731,003
2. University of California	Davis, California	NO1-HD-1-2088	Non-human Primate Breeding Colony	5/1/73-4/30/74	$164,500
			Description: Maintain a base colony of subhuman primates (species macaca mulatta) as a source of research animals of known quality for investigation whose research is supported by the National Institute of Child Health and Human Development. The nucleus breeding colony shall consist of 225 females and 25 males with at least 1/4 of the total breeding population to be maintained on an indoor timed-mated program and the rest to be kept on an outdoor random-mated program.		
	Los Angeles, California	NO1-HD-1-2215	A Study of the Growth of Mexican-American Families	1/30/73-11/30/73	32,765
			Description: Studying the determinants of fertility and family planning among Mexican-Americans in Los Angeles County. This includes design, administering and analysis of a survey.		

CONTRACTOR	LOCATION	CONTRACT NUMBER	TITLE	AWARD PERIOD	AMOUNT
	San Diego, California	N01-HD-2-2719	Synthesize and Furnish Novel Antifertility Compounds	3/1/73-10/31/73	9,231
			Description: Procure up to one gram quantities of novel 4,6-cyclopropano steroids for investigation as potential antifertility agents.		
	Los Angeles,	N01-HD-2-2778	Developmental Phenomena and the Occurence of SIDS	1/22/73-10/31/73	73,531
			Description: Continuous 12 hour polygraphic recording of EC, EOG, EMC, impedence pneumograph.		
		N01-HD-3-2716	Immune Response of Normal and Malnourished Children	2/15/73-9/14/74	94,700
			Description: Study the immunologic responses of normal and malnourished infants with emphasis on identifying changes due to nutritional deficiencies. Focus is to be given to studies of granulocytic functions in malnourished infants designed to detect defects in phagocytosis whether intrinsic granulocyte function or deficiencies in serum opsonin. Performance to take place on a pretested population in Ghana.		
	Berkeley, California	N01-HD-3-2728	Family Formations and Fertility: Key Trends and Patterns	11/1/72-9/30/73	171,088
			Description: Developing a data base to facilitate the study of the relationship between the incidence of illegitimacy in the State of California and social changes in the family and changes in sexual behavior, including abortions and venereal disease.		
	San Francisco, California	N01-HD-3-2729	Structure, Function and Development of Oviductal Cilia	1/1/73-12/31/73	29,138
			Description: Obtain information concerning oviductal cilia, their distribution, movement and function. The investigation will be conducted by means of transmission and scanning electron microscopy.		
	Los Angeles, California	N01-HD-3-2731	Effects of Steroid Contraception on Cervical Dysplasia	11/12/72-6/24/74	221,173
			Description: Continue the follow-up of the cohorts of dysplasia and normal patients. Provide a detailed description of scoring of both cytology and biopsies, description of the randomizing procedures, and repeat reading of old slides.		
	Berkeley, California	N01-HD-3-2742	Study of Oral Contraceptives and Breast Cancer	6/26/73-6/25/74	91,248
			Description: Conduct a multi-hospital case-control study of breast neoplasms to evaluate relationship to contraceptive history. Interviews shall be conducted on hospitalized women under 50 years of age, 1/4 with breast tumors, 1/4 with benign tumors, and 1/2 with other conditions that are controls.		

CONTRACTOR	LOCATION	CONTRACT NUMBER	TITLE	AWARD PERIOD	AMOUNT
	Irvine, California	N01-HD-3-2770	Postmenopausal Woman - Estrogen Therapy & Stroke Risk	6/30/73 - 8/31/74	95,900
			Description: A retrospective study of postmenopausal women with and without estrogen replacement therapy. Initial phase funded includes the development, validation, computerization and linkage of three files of a population of Leisure World residents to form the basis for the study on risks of stroke in postmenopausal women on estrogens.		
	Los Angeles, California	N01-HD-3-2776	Diagnostic and Intervention Studies of High-Risk Infants	6/30/73 - 3/22/74	480,12[illegible]
			Description: Studying premature and term infants for the purpose of establishing valid and reliable criteria for the early diagnosis of developmental fault and for assessing the effects of intervention on developmental outcome; conduct diagnostic and assessment measures on study infants, provide educational intervention to a high-risk group and analyze relation of diagnostic and intervention variables to developmental outcome at two years.		
	Los Angeles, California	N01-HD-7-1389	Steroid Contraception and Cervical Dysplasia	9/23/72 - 11/12/72	9,947
			Description: Provide a complete statistical analysis with regard to dysplasia scores as compared to other risk factors including contraceptive use. Data were compiled on a predecessor contract.		
	La Jolla, California	N01-HD-3-2765	Data Collection on Mid-Trimester Amniocentesis	6/30/73 - 6/29/74	31,405
			Description: Collect data on patients admitted to a prenatal diagnostic clinic on whom amniocentesis has been performed and in addition, data on matched control patients on whom amniocentesis has not been performed. This data will reflect the indications for the efficacy of and the safety of mid-trimester amniocentesis in the intra-uterine management of genetic-metabolic diseases.		
					$1,505,749
3. Kaiser Foundation Hospital	Oakland, California	N01-HD-3-2710	Contraceptive Drug Study	10/1/72 - 11/30/73	$818,609
			Description: Obtain longitudinal clinical and biochemical information on 17,000 women of reproductive age with reference to their use of contraceptive methods. Emphasis is on longitudinal surveillance of inpatient and outpatient data as determined from a retrospective examination of already available records for these women, prospective surveillance of inpatient and outpatient records, and annual medical examinations through an automatic multi-phase laboratory.		

CONTRACTOR	LOCATION	CONTRACT NUMBER	TITLE	AWARD PERIOD	AMOUNT
4. Professional Staff Assoc. of LAC/USC Medical Center	L.A. Calif.	N01-HD-1-2455	Research on Intrapartum Fetal Monitoring Description: Conduct a clinical investigation of high risk pregnancies by correlating bio-physical and biochemical findings which occur during the intrapartum period and the first 24 hours of extra-uterine life. A fetal high-risk index will be developed which takes into consideration the clinical maternal risk factors, baseline fetal heart rate, abnormal heart rate patterns, acid base status of the fetus, and uterine activity.	10/1/72-12/31/73	$455,400
		N01-HD-3-2757	Collaborative Study of the Effects of Vasectomy Description: Select and conduct on 50 vasectomized men and 50 controls comprehensive medical inventory and physical examination, urological examinations and psychological evaluations from prior to surgery to 12 months thereafter. Conduct on 25 patients and 25 controls various serum level tests and sperm agglutinating and sperm immobilizing antibody determinations. Conduct appropriate statistical analyses.	6/30/73-12/31/74	337,000
					$792,400
5. University of Washington	Seattle, Washington	N01-HD-3-2791	Detection of Ovulation in Animals Description: Designed to develop electronic hardware which can detect the passage of ova through the oviduct. This can serve as an accurate method of ascertaining the time of ovulation. The initial work is to be done in rabbits and then it will be attempted in primates.	1/17/73 - 6/14/74	119,040
		N01-HD-3-0433	Conference Contract Symposium on the biology and pathology of aging gametes	12/4/72 - 12/3/74	29,178
		N01-HD-3-2788	Biology of the Oviduct and Gamete Transport Description: Define the role that the oviduct plays in the movement of ova and sperm and the subsequent propulsion of the fertilized ovum. The contract involves cinematographic recording and the development of transducers to monitor oviductal function.	6/3/73-6/2/75	402,801
		N01-HD-3-2793	Hearing Impairment and Language Disability Description: Preparing methodological tools necessary to investigate the nature of normal language development in very young children and concerning the impact of hearing impairment and Down's Syndrone on language developments.	6/15/73-12/14/74	219,892
					$770,911

CONTRACTOR	LOCATION	CONTRACT NUMBER	TITLE	AWARD PERIOD	AMOUNT
6. Pennsylvania State University	University Park, Pa.	N01-HD-1-2228	Assay of Progesterone Receptor Activity in the Uterus	3/6/73-6/27/75	$86,776
			Description: The development of an *in vitro* receptor assay for the competitive binding of progestational and antiprogestational agents. The intent is to rapidly screen compounds for antiprogestational activity which may have contraceptive potential.		
		N01-HD-2-2730	Comparative Study of Progestin Metabolism in Animals	2/27/73-7/31/74	401,985
			Description: Conducting a comparative study of progestin metabolism and the mechanism of action in experimental animals. This is part of a comparative pharmacological program to determine if certain agents effect all species similarily.		
		N01-HD-9-2137	Role of the Epididymis in Sperm Maturation	6/23/73-6/22/75	156,685
			Description: Characterize testicular, cauda epididymal, and ejaculated sperm and their surrounding fluids to detect biochemical or metabolic differences which might suggest vectors or targets for a male contraceptive.		
					$645,446
7. Pan American Health Organization INCAP	Guatemala City, Guatemala	N01-HD-2-2737	Data Analysis-Ecological Study in a Guatemalan Village	6/1/73 - 5/31/74	$ 64,450.
			Description: Analyze and publish data from a longitudinal study of nutrition, infection, and growth among pregnant and lactating women, infants, and children.		
		N01-HD-5-0640	Nutrition Survey Among Indian Groups in Guatemala	3/1/73 - 2/28/74	$543,685.
			Description: Conduct a longitudinal study of nutrition and child development in four isolated Guatemalan villages paired on socio-economic and other variables. Measurements will include nutritional status, health and morbidity, psychological development, and changes in the social environment. Emphasis shall be on the methodological analysis and the systematic elaboration of models for longitudinal analyses of the effects of nutrition and mental development.		
					$608,135.

CONTRACTOR	LOCATION	CONTRACT NUMBER	TITLE	AWARD PERIOD	AMOUNT
8. **University of Texas**	Galveston Texas	N01-HD-2-2728	Sex Steroids and Nutritional Status Description: Assess the effects of estrogens and progestins on the nutritional health status of 800 contraceptive users in cross sectional and longitudinal studies. Report on baseline studies to determine variations of biochemical nutritional parameters during the menstrual cycle.	6/30/73-6/29/74	$114,600
	Dallas Texas	N01-HD-2-2756	Estrogen Studies in the Postmenopausal Woman Description: Studying postmenopausal women to determine the sources of estrogen in the body, how it is synthesized and the quality of estrogen produced. It is an attempt to relate the findings to the process of aging and age associated diseases.	6/15/73-6/14/74	105,000
	Austin Texas	N01-HD-3-0779	Conference - Population Area Description: Conference on the Mexican-American population. This was a demographic to consider the trend of fertility and related variables with respect to Mexican-Am Trends are compared to those of the total U.S. population.	3/19/73 - 3/18/74	11,011
	Austin Texas	N01-HD-3-2708	Demography of the Black Population Description: Describing and analyzing trends and demographic characteristics of the Black population and comparing these with trends in the White population through an analysis of published census data.	9/1/72-8/31/74	87,792
	Houston Texas	N01-HD-3-2779	Specific Cytoplasmic Receptors in Human Cervical Tissue Description: Analysis of information about the presence, nature, and function of estrogen and progestogen receptors in the human cervix, which would help in formulating methods of birth control.	6/30/73-6/29/75	71,981
	Houston Texas	N01-HD-3-2782	Localize and Identify the Androgen Receptors in the Testis Description: Conduct of studies to establish the presence of androgen receptors in testes, their specificity, their fate, and the effect of synthetic androgens and anti-androgens on the normal course of events in target cells which may yield valuable basic biochemical information as to points of androgen control.	6/30/73-6/29/75	96,706

CONTRACTOR	LOCATION	CONTRACT NUMBER	TITLE	AWARD PERIOD	AMOUNT
	Galveston Texas	N01-HD-9-2139	Ultrastructural, E/M Studies of Mammalian Spermiogenesis	6/19/73-6/18/74	88,533
			Description: Investigations concerning the ultrastructural cytochemistry of mammalian spermatogenesis, which may provide targets for altering or control of fertility.		
	Houston, Texas	N01-HD-9-2221	Specific Binding of LH in the Corpus Luteum	2/15/73 - 11/18/73	$ 19,754.
			Description: Synthesize 0.5 grams of ovine LH subunits for reproductive biological investigations; milligram quantities of derivatives of LH and its subunits for investigation as potential antifertility agents, and a biochemical study of the properties of the chemically modified LH and LH subunits.		$595,377.
9. University of Tulane	New Orleans, La.	N01-HD-2-2713	Studies of Small Peptides which Release LH and FSH	3/15/73 - 3/14/74	$110,577.
			Description: Synthesize milligram quantities of novel analogs of luteinizing hormone releasing hormone and the biological evaluation of these peptides as potential antifertility agents.		
		N01-HD-2-2741	Synthesize and Evaluate Analogs of LH-RH/FSH-RH	6/30/73 - 6/29/74	$ 73,268.
			Description: Synthesize milligram quantities of novel analogs of luteinizing hormone releasing hormone and the biological evaluation of these peptides as potential antifertility agents.		
		N01-HD-2-2788	Relationship of OC's to the Nutritive State	3/5/73 - 6/29/74	$110,916.
			Description: Examine the nutritional status of 50 new and 100 longtime users of oral contraceptives who are potentially a high risk nutritionally. Results shall be compared with two matched control groups who use other methods of contraception.		
		N01-HD-3-2758	Immunologic and Morphologic Effects of Vasectomy	6/1/73 - 3/31/75	$278,335
			Description: Study immunologic responses and morphologic changes in the testis, epididymis and vas deferens after vasectomy in Rhesus monkeys and determine the role of extravasation of sperm in initiation of an immune response.		$573,096.

CONTRACTOR	LOCATION	CONTRACT NUMBER	TITLE	AWARD PERIOD	AMOUNT
10. Research Triangle Institute	Research Tri. Park, N. C.	NO1-HD-2-2712	Synthesis of Prostaglandin Analogs	4/1/73 - 6/29/74	$ 73,551.
			Description: Synthesize milligram quantities of novel prostaglandin analogs for investigation as potential antifertility agents.		
		NO1-HD-2-2716	Synthesis and Testing of Silicon Substituted Steroids	4/1/73 - 6/29/74	$ 56,890.
			Description: Synthesize 100 to 500 milligram quantities of silicon substituted steroids for investigation as potential antifertility agents.		
		NO1-HD-3-2741	Biodegradable Polymers & Delivery of Contraceptive Drugs	5/15/73 - 5/14/75	$296,811.
			Description: Develop biodegradable polymers and determine whether these polymers can be utilized as carrier systems for the sustained (prolonged and uniform) deliveryof contraceptive drugs.		
		NO1-HD-3-2747	Synthesize Ring A Bicyclo-Steroids	4/23/73 - 4/22/74	$ 26,860.
			Description: Synthesize 500-1,000 milligram quantities of novel ring A bicyclo [2.2.0] steroids fo investigation as potential antifertility agents.		
		NO1-HD-3-2748	Inhibitors of Uterine Estradiol Binding Factors	4/9/73 - 4/8/74	$ 64,490.
			Description: Synthesize 100-200 milligrams of similar modifications of 19-nor progesterone and 17α-ethynyl-19-nor testosterone for investigation as irreversible inhibitors of uterine progesterone binding factors and potential antifertility agents.		
					$518,602.

RELATIONSHIP WITH OFFICE OF HUMAN DEVELOPMENT

Mr. **Flood.** What is the division of effort between the National Institute of Child Health and Human Development and the Office of Human Development?

Dr. **Corfman.** Office of Human Development or the Office of Child——

Mr. **Flood.** You have National Institute of Child Health and Human Development over here and then you have the Office of Human Development.

Mr. **Hedetniemi.** The Office of Human Development at the Secretary's level provides a coordination and planning function for the department, whereas our function is essentially in biomedical research.

Mr. **Flood.** You are operational?

Mr. **Hedetniemi.** Yes.

RESEARCH ON THE LIVING FETUS

Mr. **Flood.** What is the current National Institutes of Health policy with reference to research on the living fetus?

Dr. **Corfman.** As of now——

Mr. **Flood.** As of half past 3 this afternoon what is it?

Dr. **Corfman.** Do you want to answer that, Dr. Stetten?

Dr. **Stetten.** There is no definitive policy at this time but one is being developed. It has been published, as a proposal, in the Federal Register.

Dr. **Lowe.** The guidelines on human experimentation were set in 1966. The guidelines published as a policy statement by the National Institutes of Health in 1966 still form the backbone of all policy decisions with respect to this issue including the human fetus.

At the present time a memorandum has been written which prohibits review or funding of research grant applications or contracts which deal with a human fetus delivered by abortion. But this is a current prohibition which eventually may or may not be modified, and it is the only substantial change in the 1966 policy guidelines.

Mr. **Flood.** Delivered by abortion?

Dr. **Lowe.** Yes, sir.

MULTIYEAR GRANTS AND OBLIGATIONS OF RESTORED FUNDS

Mr. **Flood.** Add these things for the record. On page 51, a revised version of that table reflecting the 1973 funds obligated in 1974 and then the 1974 funds obligated for a 2 year period, and also a statement of the use of the 1973 funds released from impoundment, and a statement about the 2 year grants made from the 1974 funds.

[The information follows:]

Obligations by Budget Mechanism Showing "True" Program Levels in 1974 - 1975
(Amounts in thousands)

Budget Mechanism	1972		1973		1974		1975	
	No.	Amount	No.	Amount	No.	Amount	No.	Amount
Grants								
Regular								
Noncompeting	508	$31,648	630	$39,655	608	$40,186	833	$54,859
Competing	103	7,177	75	5,713	129	11,244	55	4,621
New	296	15,368	174	9,300	315	16,710	140	8,660
Supplemental	(20)	470	(32)	422	(20)	340	(20)	340
Subtotal	907	54,663	879	55,090	1,052	68,480	1,028	68,480
Special								
Mental retardation res. ctrs.	12	5,608	12	5,608	12	5,608	12	5,608
Research career programs	117	2,787	106	2,595	93	2,439	82	2,146
Scientific evaluation		155		155		155		182
Subtotal	129	8,550	118	8,358	105	8,202	94	7,936
Total research grants	1,036	63,213	997	63,448	1,157	76,682	1,122	76,416
Fellowships								
Noncompeting	31	297	34	341	20	280	214	2,897
Competing	1	13	1	8	3	24		
New	57	555	9	121	221	2,792	153	2,065
Supplemental								
Subtotal	89	865	44	470	244	3,096	367	4,962
Training grants								
Noncompeting	81	7,555	85	6,266	60	6,693	87	7,955
Competing	23	1,724	6	409	25	2,458		
New	7	409	2	92	8	904		
Supplemental	(28)	454	(6)	138				
Subtotal	111	10,142	93	6,905	93	10,055	87	7,955
Intramural, laboratory & clinical research:								
Laboratory & clinical res.		11,596		12,325		13,519		14,012
Biometry, epidemiology & field studies		386		628		706		715
Research & devel. contracts		20,300		18,952		20,497		20,668
Research mgmt. & program servs.		5,990		7,001		8,325		8,532
Total		112,492		109,729		132,880		133,260

Obligations by Budget Activity Showing "True" Program Levels in 1974 - 1975

(Amounts in thousands)

Budget Program	1973		1974		1975	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Population	--	$34,768	--	$42,960	--	$43,249
Child Health	--	46,608	--	56,592	--	56,028
Aging	--	8,399	--	10,778	--	10,724
Intramural, Laboratory & Clinical Research	358	12,953	338	14,225	348	14,727
Research Management and Program Services	199	7,001	181	8,325	181	8,532
Total	557	109,729	519	132,880	529	133,260

Multi-Year Funding from 1974 Appropriation

(Amounts in thousands)

Budget Mechanism	No. of Awards	Total Amount	Amount Affecting 1975 Funding	Remarks
Research Grants	112	$13,341	$6,670	Total
	39	5,231	2,615	Population
	50	5,170	2,585	Child Health
	23	2,940	1,470	Aging
Fellowships	27	562	281	Total
	6	128	64	Population
	19	393	196	Child Health
	2	41	21	Aging
Training Grants	13	1,924	962	Total
	2	462	231	Population
	9	1,216	608	Child Health
	2	246	123	Aging
Research & Development Contracts	7	901	450	Total
	1	113	57	Population
	5	723	361	Child Health
	1	65	32	Aging

Distribution of 1973 Impounded Funds
(Amounts in thousands)

Budget Mechanism	No. of Awards	Amount	Remarks
Research Grants	141	$ 8,716	Total
	51	3,261	Population
	81	4,860	Child Health
	9	595	Aging
Fellowships	68	635	Total
	42	388	Population
	22	213	Child Health
	4	34	Aging
Training Grants	20	4,693	Total
	8	1,250	Population
	10	2,718	Child Health
	2	725	Aging
Research & Development Contracts	21	2,249	Total
	16	1,590	Population
	4	559	Child Health
	1	100	Aging

Mr. Flood. Mr. Casey.

EXTENSION OF TITLE X AUTHORITY

Mr. Casey. Thank you, Mr. Chairman.

In your justification on page 36 you state that no title X funds will be used and you are not asking for an extension of title X, which will expire in June 1974, I believe. I understand that the House Interstate and Foreign Commerce Committee is planning to extend it.

Title X, as you know, prohibits the use of any funds for family planning services or population research where abortion is used as a means of family planning. Why do you propose to stop funding your program under title X?

Dr. Corfman. I would like to give two responses. The first is technical in that we do not need the authorization from title X because we have it under title IV.

Mr. Casey. Title X was not necessary for the funding?

Dr. Corfman. No, sir. But my second response involves your concern for abortion. Section 1008 of title X says none of the funds from title X will be used for abortion as a form of family planning. Even though that section doesn't apply technically to NIH, we recognize it as reflective of the intent of Congress, and our Institute has been very careful not to support research where abortion is used as a form of family planning. However, we do have research projects on attitudes toward abortion, the medical consequences of abortion, and abortion statistics.

SOCIAL SCIENCE PROGRAMS

Mr. Casey. You did mention that you have several programs in the social sciences?

Dr. Corfman. Yes.

Mr. Casey. What progress are we really making in population research?

Dr. Corfman. I shall start with our social science program. Data from our Institute were the backbone for many of the recommendations of the Presidential Commission on Population Growth and the American Future. I refer to the significant differences between the two- and three-child family in our future development; studies on the attitude of couples toward children and their preferences concerning the number of children; work on the role of women.

Mr. Casey. You say you made studies of the difference between a two-child and a three-child family?

Dr. Corfman. That is a significant difference. If Americans continued to have three children——

Mr. Casey. Have you made a study between a 2-child family and a 10-child family and see how they do?

Dr. Corfman. I am describing such work as examples of progress in population research. The Institute has obtained data which have been important to our country's population policy.

Another example is our work on the medical effects of contraceptives, particularly oral contraceptives. We know a great deal more than we did 3 years ago about the incidence of stroke, about effects on blood pressure, and the effects of the oral contraceptives on nutrition. We are beginning to get information on the medical effects of vasectomy, a program we started 2 years ago.

I would say we also have made good progress in our efforts to develop new contraceptives. The last part of our program is called fundamental research essential to the field. It is the backbone of the program and we have made tremendous progress in such fields as the mechanism of hormone action.

INSTITUTE STUDIES ANALYZING EUROPEAN DATA

Mr. Casey. On page 4 of your statement you say, "recent institute studies analyzing European data."

Dr. Corfman. Yes.

Mr. Casey. Where did you get the European data? How did you accumulate it?

Dr. Corfman. It is data from Czechoslovakia.

Mr. Casey. Something we financed?

Dr. Corfman. The work was done by American scientists on data they obtained from Czechoslovakia.

Mr. Flood. If the gentleman will yield, when you say Czechoslovakia, you know the composition of the republic, the different national units. Is that part of the program? Czechoslovakia. Do you know if there was something peculiar or special about that?

Dr. Corfman. We have a paper describing the work in detail.

Mr. Patten. He is head of the captive nations program in the Congress.

Mr. Flood. If you don't know off the top of your head, have the record show it.

Dr. Corfman. We shall put an abstract on the study in the record.

[The information follows:]

Summary of NICHD-Supported Research on Outcome of Unwanted Pregnancies

A large number of pregnancies are unwanted. Therefore, it is very important to discover how this affects the individuals who result from such pregnancies.

Dr. Henry David conducted the first study which was able to compare systematically the physical, mental, social, and educational development during the first 8 to 9 years of life of matched experimental (unwanted) and control groups of children born in 1961–63. The unwanted children, those born to women twice denied abortion (initial request and appeal), were matched with a control group of the same sex, age, birth order, and school class whose mothers planned to have the child or did not request abortion. The mothers were also appropriately matched.

Czechoslovakia presented excellent opportunities for conducting the study. Since 1958, abortions on request have been legal. Although the law is liberal, approximately 8 percent of women are denied abortion on initial request and 3 percent remain disapproved on subsequent appeal. This allows for an operational definition of unwanted pregnancy. In addition, quite a large number of routinely prepared, sequentially timed public health medical records, educational records, and other objective informational materials are maintained. It was possible also, because of the careful maintenance of extensive records, an initial pilot study, and the central population register to locate unwanted and control groups and their parents. This made possible intensive studies of the children and their parents about 8 or 9 years after birth.

Current comparative findings are based on 100 children in each group (wanted and unwanted) and more data will be forthcoming.

The results to date support the hypothesis that children who are unwanted at pregnancy do not appear to do as well as wanted children in several aspects of development, such as social, psychological, and educational aspects.

Some observed differences are briefly given below.

(*a*) On the average, mothers of unwanted children breast-fed their babies a shorter time.

(*b*) During the preschool years, the unwanted children were more frequently ill, injured, operated on, and hospitalized.

(*c*) Even though the two groups did not differ in measured intelligence, the unwanted group performed more poorly in school.

(*d*) During the preschool age, the u nwanted are more aggressive, angry, irritable, assertive, and self-centered. During school age, these kinds of differences are still more in evidence. The unwanted seem to be living under some stress and to get along poorer within the family.

Mr. CASEY. I wonder why you use European data rather than data from our country?

Dr. CORFMAN. The intent of the scientists was to try to find what happens to children that are unwanted, and the fact is that the best data for such work comes from such a country.

Mr. FLOOD. The Slovak is traditionally a very high Roman Catholic entity.

Dr. CORFMAN. Mr. Casey asked me why this work on data from Czechslovakia rather than the United States. They have a large number of patients who can be studied and a good record system.

Mr. CASEY. In the European data, you mention the study of offspring of mothers who had been denied abortions twice. Why would they be denied, abortions are legal over there?

Dr. CORFMAN. By twice denied we mean that the women were forbidden an abortion both on first request and on appeal. They were turned down for medical reasons such as having had a recent abortion.

Mr. CASEY. In other words, the woman thought she didn't have to worry anymore, that she could always get an abortion, but they turned her down on the third trip. Is that it?

Dr. CORFMAN. They turned the women down for medical reasons.

Mr. PATTEN. You mean it could be a heart condition or high blood pressure?

Dr. CORFMAN. I think the primary reason for turning them down was if they had had a recent abortion.

Mr. CASEY. In other words, they reverse it over there. The test is not whether an abortion is necessary for her health or well being, but they deny it if they believe an abortion will affect her health or well being. Is that it?

Dr. CORFMAN. Yes.

ABORTION

Mr. CASEY. It is a reverse situation. You are not then considering abortion as a type of family planning in your operation?

Dr. CORFMAN. No, we are not using any of our funds to promote abortion as a form of family planning.

Mr. CASEY. You say, "not to promote." Are you doing research on abortion as a means of family planning?

Dr. CORFMAN. No, we are not. I would be happy to supply a list of our abortion projects for the record. You will see that they are limited to studies of the medical effects of abortion, particularly criminal abortion, and sociological studies.

Mr. CASEY. Put that in the record: What the abortion projects are and what their purpose is.

Thank you, Mr. Chairman.

[The information follows:]

ABORTION PROJECTS

FY 1973

<table>
<tr><th>Grant Number</th><th>Investigator Institution Location</th><th>Title</th><th>Funds</th></tr>
<tr><td>R01 05853</td><td>Diamond, Milton
Univ. of Hawaii
Honolulu, Hawaii</td><td>Pregnancy, Birth Control and Abortion</td><td>$73.546</td></tr>
<tr><td></td><td colspan="3">There are two general objectives of this research: (1) to assess the social, demographic, behavioral, medical and public health effects of the legalization of abortion in Hawaii and (2) to analyze the correlates and processes of decision-making regarding sexual intercourse, contraceptive use and planning for pregnancy, and pregnancy outcomes when abortion is legal. The investigator aims to detect changes over the three-year period since the legalization of abortion, and to locate those factors which remained stable during the same time frame. Hospital records, questionnaires and interviews constitute the source of data.</td></tr>
<tr><td>R01 05952</td><td>Perez-Reyes, Maria
Univ. of North Carolina
Chapel Hill, N.C.</td><td>Follow-up of Abortion or Motherhood in Adolescence</td><td>42,653</td></tr>
<tr><td></td><td colspan="3">This is a longitudinal research project on: (1) psychological, social and educational factors involved in uneventful pregnancies of young adolescents; (2) the factors involved in making the decision about the outcome of the pregnancy and (3) the after effects of therapeutic abortion and full term pregnancy. The sample which will be racially mixed consists of 13-16 year old girls from various socio-economic classes. The data are collected from interviews, questionnaires and psychological tests.</td></tr>
</table>

R01 06095 Stycos, J. Mayone, Diocesan Mobilization Against Abortion Law Reform $ 13,092
Cornell Univ.
Ithaca, N.Y.

The dioceses of New York State are being studied for variations in the manner and intensity with which they oppose the New York 1970 abortion law. The study includes careful examination of the areas of mobilization--political, educational, and service--, and comparison of diocesan intensity within these areas; the structural and environmental factors responsible for diocesan mobilization and how the New York State Catholic Committee is coordinating the individual mobilization of the eight dioceses. In-depth interviewing mailed questionnaires, and anlysis of the content of documents of the various organizations will provide the data for the study.

R01 06152 Steward, Phyllis L. Normative Views of Physicians Performing Abortion 13,004
George Washington Univ.
Washington, D.C.

The purpose of this study is to examine physicians' normative attitudes on abortion in general, on repeated abortions and on the use of abortion as a means of birth control. It would be a descriptive study of the emerging guidelines used by physicians in responding to requests for abortion as a birth control method as opposed to contraception. The data are collected from a larger abortion questionnaire being fielded by the Institute for Survey Research at Temple University and from self-administered questionnaires distributed among a sample of obstetricians and gynecologists in the Washington, D.C. area.

R01 06830 Welcher, Wayne H. Effect of Therapeutic Abortion on Unmarried Women 20.381
Ventura General Hospital
Ventura, Calif.

The objective of this research is to conduct a one-year follow-up study of the behavioral effects of therapeutic abortion among never married pregnant women. The outcome of abortion will be compared to the changes observed among women who do not have their out-of-wedlock pregnancies interrupted, but marry and carry to term or become single parents. The study will attempt to determine why pregnant single women choose one alternative rather than another, how they are affected by their decisions, and whether or not they prevent subsequent out-of-wedlock pregnancies. Information is collected by interview at the time of the initial visit, the post-partum visit, and six months later.

R01 07214 Shachtman, Richard 'Long-term Complications of Induced Abortions $21,880
Univ. of North Carolina
Chapel Hill, N.C.

This is a study of long-term complications such as infertility, prematurity, stillbirth, mortality, etc. which may be due to induced abortions. The objective is to obtain reasonably accurate statements of such long-term risks for at least some of the possible complications by use of stochastic models. The main approach for this analysis is a carefully aggregated Markov chain model.

R01 07388 Budner, Stanley Correlates of Abortion Seeking Decisions 35,506
Columbia Univ.
New York, N.Y.

The primary goal of this study is to explicate the demographic situational and psychological factors affecting the perceived need for and the steps taken to obtain an abortion. The analysis has three major goals: (1) to develop a picture of abortion seeking in terms of the decision tree model; (2) to prepare reports of interest to professionals in public health and abortion research, and (3) to link abortion behavior to general social science concepts and theories.

K06 20169 Csapo, Arpad Istvan Maintenance and Termination of Pregnancy 31,238
Washington Univ.
St. Louis, Mo.

This career award provides salary only to an investigator who carries out the following clinical studies concerning induced abortion: (1) the mechanism of abortifacient action of prostaglandins and (2) the effect of luteectomy during first trimester pregnancy.

N01 12142 Lo Sciuto, Leonard A. A Study of Physicians' Attitudes Toward Abortion 44,000
Temple Univ.
Philadelphia, Pa.

The major purpose of this study is to assess physicians' current perceptions, understandings, and attitudes toward birth control methods which may be considered as possible abortifacients. The doctors' attitudes concerning criminal as well as legal (therapeutic) abortions and relevant general attitudes toward fertility intervention and birth control are also examined. Data are collected from interviews given to a national probability sample of doctors and osteopaths whose practice makes the subject of fertility control a reasonable occurrence.

Mr. Flood. Mr. Patten.

Mr. Patten. Sitting here I am reminded of coming out of church after listening to a big missionary blast off about the duty of the mother. They are very effective. Coming out I saw Mrs. Hennessey who had nine children. I said to her, "What did you think of the missionary?" She said, "I wish I knew as little about it as he does."

LEUKEMIA TRAUMA

So I often wonder how little we know of the real social aspects of this population business. There is a headline here in today's Star that says "Leukemia trauma." It says, "Only 1 family in 10 who loses a child to leukemia emerges from the experience without serious marital problems, suicide or divorce, disturbed child-parent relationships" and things of that type.

In my lifetime I have seen that so often. You can call it. It seems if you have a defective child born there are so many other factors and it is devastating.

In your studies do you consider the social aspects? This article would suggest there is a trauma after a child has died of leukemia.

Dr. Corfman. The same kind of article could be on the effects of a sudden infant death.

Mr. Patten. I know a fellow lost his son and for 7 years he wasn't right. Before that he was the top man in a civil service examination taken by 800; No. 1. A few years after he lost his child he just couldn't go to work.

While we are talking about the social aspects of abortion or anything else, I was in Hungary in a day nursery with these wonderful people. But no Gestapo around. And the women told me that in Hungary they had the highest suicide rate in the world, that they had the lowest birth rate in the world. There were a number of women there. They kept the place very clean as you know. I wish all of our facilities here were as clean and immaculate and as well tended by intelligent people.

I happened to ask the woman whether she had children. She said to me "Who would bring a child into the world in this country?"

So you are speaking of your Czechoslovakian report. You know the high regard I have from personal knowledge of Slovaks. They don't come any better. They are wonderful people. I have a lot of them in my district. America would be great if we had only Slovaks. They are intelligent, industrious, clean, decent.

I would have to know more about that as to whether it was when the German tanks were in there, at what stage of the affair this report was made. If like that poor Hungarian feels with the Russian Army running Hungary, there is no use, or no sense to bring a child into the world, it is a different ball game.

Incidentally, the figures on suicide are by the U.S. Department of Labor, and the Hungarian Government issued the figures about the highest suicide rate and lowest birth rate.

I was interested in something else you said because it is contrary to what a couple of my baby doctors told me from time to time.

Dr. Corfman. I think you are asking whether infant mortality is genetically determined and I would say no in the context of your question.

CELL BIOLOGY

Mr. PATTEN. I am just going to make one more observation. A fellow my age ought to lay in bed and dream of Aladdin's lamp and the fountain of youth. You tell me you old fellows are changing your theories and if we solve our aging problem it is going to be based on cell biology if I remember your words.

Dr. CORFMAN. Cell biology, molecular biology, the learning process, immunology, all are examples of fundamental research.

Mr. PATTEN. For a general statement, not being specific, I read there that the scientists are beginning to change and think if we get the answers to the aged we are going to have to be in the field of cell biology. I think I read that in the justification.

Dr. CORFMAN. I think Dr. Stetten would agree that to get answers to many problems in medical research we have to go to the cell.

Dr. STETTEN. We must reduce them to that level.

Dr. CORFMAN. In addition to molecular and cellular biology, we are doing many other important things in our program.

SENILITY

Mr. PATTEN. The chairman mentioned senility. I have seen people do something about senility and get results and have a changed person.

Mrs. Moore signed a deed for me not long ago. She is 93. She didn't even wear glasses. She is hard of hearing but otherwise she seems to be as sharp as a bell. You see things that really surprise you.

I was hoping when I got to my present age, 68, you fellows would come up with something so the next 20 years would be a little more beautiful.

You say from over 65 most of us have one serious physical handicap, right?

Dr. CORFMAN. Yes.

PREVENTIVE CARE

Mr. PATTEN. We know it is true. I think if we are going to have 40 million people over 65 years of age in this country in the next couple of decades we ought to do more than what we are doing in preventive care. Because if you figure the cost, social security, medicine, hospitalization, nursing homes, all the other costs, it must be in the many billions.

Do you know what they charge at a nursing home? They want $175 a week. Many can't afford to be old. I think old age is a disease.

That is enough, Mr. Chairman.

Mr. FLOOD. Mr. Obey.

INFANT MORTALITY

Mr. OBEY. Thank you, Mr. Chairman.

Doctor, on page 3 of your statement you mentioned the new facility at NIH for expanded research in areas of pregnancy and infant mortality and morbidity. Are you assured of adequate positions to staff this facility without their being taken from other activities?

Dr. CORFMAN. The 10 new positions we expect to have in 1975 will all be assigned to that program directed by the only other full-time obstetrician at NIH. I would say that 10 is sufficient to get the program under way. We are currently discussing with the Department the allocation of additional positions to bring this facility into full use.

Mr. OBEY. Ten is sufficient this year without taking people away from other activities?

Dr. CORFMAN. For the first year, yes.

SUDDEN INFANT DEATH SYNDROME

Mr. OBEY. Everybody has mentioned sudden infant death syndrome. I don't know if my information is correct on this or not. There is obviously a public desire for much greater research in this area, but it has been my impression it has been somewhat difficult for you to expand your research program in that area. Am I right or am I wrong?

Dr. CORFMAN. It has expanded. We project $4.7 million for fiscal year 1975. It has been difficult to get people to do the work in this field because so little is known. My colleagues at NIH have done a remarkable job in doing just what a science manager should do, and that is to generate an interest in socially important fields and to categorize the problems so they can be attacked in the laboratory, and once good projects are developed, to fund them. A program which was almost nonexistent 3 or 4 years ago and is now almost $5 million shows considerable growth. That is something to point to with pride.

AGING

Mr. OBEY. Let me ask you again. Everyone else has mentioned it would appear, at least to me, to be an inadequate budget for research on aging. You are spending at virtually a level level if not somewhat less than last year.

Dr. CORFMAN. In fact we have an increase $107,000 in the program level of aging research. This is not a cut but a slight increase. But inflation will eat up that increase.

Mr. OBEY. I said a level level, and in the world of rising prices if you remain level, you are cutting the program.

Dr. CORFMAN. Right. This is the budget we feel is adequate to our needs. In fact the Institute is responsible for studying the normal aging process. We deal very little with specific diseases since they are studied by other institutes.

Mr. OBEY. Let me argue with that point a little bit. You point out in your statement that since 1900 the average lifespan in this country has increased from 49 to 71 years. Dr. LaVeck pointed out last year in his testimony that in that same period of time we have only extended the life expectancy of the 50-year-old white male by 2 years. If you look at your own justifications on page 72, it says "Mounting public concern about the impact of environmental and nutritional factors on life and health mandates further emphasis in 1975 on aging research in these areas."

On page 73, "It has recently been discovered that there is a striking diminution in immunological competence with increasing age. The decline is so great that the elderly retain only one-tenth of the peak immune capacity shown during adolescence. The marked deterioration in immune function that occurs with age is important because it predisposes the middle-aged and elderly to infections, cancer, and autoimmune disease."

In your own statement at the bottom of page 7 you mention "The immune system may also protect from challenges within the body such as cancer cells."

It would seem to me with all of the effort that is being put on cancer research that an argument could be made for an increased budget for research on specific problems in the aging.

Dr. CORFMAN. I certainly agree with you. I hope the exciting leads in such fields as immunology being made in our own laboratories and in the extramural program will be followed up in subsequent years.

Mr. OBEY. In subsequent years. With all of the assertions made in the justifications and in your statement and in light of the fact we have only increased life expectancy once you get into middle age by a couple of years, I find it difficult to buy your apparent assertion that the amount of money in this Institute for research on aging is adequate.

Dr. CORFMAN. No programs in research are ever adequately funded. What we have presented is what we consider to be the best balance among our three program responsibilities.

Mr. OBEY. When I compare the amount of money that you are spending for population control with the amount spent on aging it does seem to me as a layman to be somewhat out of balance.

Dr. CORFMAN. I cannot accept that.

Mr. OBEY. That is all, Mr. Chairman.

COORDINATION WITH OTHER INSTITUTES

Mr. CONTE. Since your programs cover the whole life span, they are bound to overlap with all the other programs of NIH and with the Office of Human Development and NIMH. Do you have some formula for sorting out your interests, or do you negotiate on a case-by-case basis?

Dr. CORFMAN. There are indeed several areas of overlap between NICHD and NIMH as well as other Institutes within NIH. These are resolved for the most part by having research grant applications for NIH and NIMH processed through the Division of Research Grants. A Handbook of Referral has been established which describes the mission, research interests, and special programs of each Institute and of NIMH. The Division of Research Grants assigns each application to the appropriate Institute based on these guidelines. In those cases where overlap cannot be easily resolved, the staff members may be asked to provide additional information or opinions.

Overlap with the Office of Human Development also may exist. OHD does not use the DRG system nor has it prepared a detailed description of its research interests. However, in general, the OHD mission is different than NICHD—with a greater emphasis on intervention programs and systems rather than on more basic underlying processes.

CHILD ABUSE

Mr. CONTE. Congress has expressed great concern with the problem of child abuse. Are you looking into this at all?

Dr. CORFMAN. Yes; one of the best ways to understand, and to possibly prevent deviant and pathological parent-child relationships that sometimes result in child abuse or neglect is a thorough understanding of normal parent-child relationships and the conditions that support and promote them. To this end, this Institute has awarded during fiscal year 1974 two new research contracts and one new research grant that are relevant to the matter of child abuse and neglect. Another such research grant has been given Council approval and will be funded in fiscal year 1974. The total estimated research grant and contract funds will be approximately $248,000.

The NICHD will also convene a conference in June of this year on the problems of conducting research on the effects of child abuse and neglect on the later development of children, as well as research problems in other biomedical areas relevant to child abuse.

NUTRITION

Mr. CONTE. Your justification seems to hint that some areas you've been supporting in the field of nutrition are at a dead end. Is this so? Which are they?

Dr. CORFMAN. We're sorry if we gave you that impression. The converse is more nearly true. Nutrition research is moving forward very rapidly in a number of areas. Examples would include the role of malnutrition in mental development, resistance to infection, and pregnancy outcome and low birth weight; other areas of great current interest are the requirements for feeding premature babies and the origins of obesity. Still other areas which have been somewhat dormant in recent years are now being stimulated. These include adolescent nutrient needs and the role of nutrition in the aging process.

Mr. CONTE. Are you interested in the relation between eating habits in children and food advertising, particularly on television?

Dr. CORFMAN. NICHD is not supporting studies on children's eating habits and how they may be influenced by advertising.

CHILD DEVELOPMENT

Mr. CONTE. Especially in young families, fathers seems to be taking a bigger part in care of small children. Does this have any effects on child development?

Dr. CORFMAN. The Institute is supporting a study of the way fathers from diverse social backgrounds interact with their 4-year-old children under natural conditions and the relation of these different styles of interaction to the child's intellectual and personality functioning. Since this study began in September, 1972, and will not be completed until September, 1975, the final results are not yet available. But one can expect that the style, as well as the amount of caretaking, will have an influence.

The Institute has also been studying patterns of parental authority for a number of years. The subjects were 4 years old when the project started and they are now 8 and 9 years old. We will follow these subjects, with additions, for the next 4 years. This longitudinal study provides a natural experiment to detect changes in the father's involvement in family interaction. The actual result of these changes will not be known until the study is completed.

Mr. CONTE. What about children who spend their earliest years in the kinds of communes we've seen springing up in the last few years. Do you have any studies on how these affect children?

Dr. CORFMAN. The NICHD does not support any study of the effects of childrearing practices in the various types of communes which have sprung up in the last decade.

HANDICAPPED CHILDREN

Mr. CONTE. There have now been a number of court cases to force school systems to provide appropriate education for the handicapped child, including the retarded. Is the Institute providing any consultation to school systems? Do you have any studies of the effects, good or bad, of putting retarded or hyperactive children in regular classrooms?

Dr. CORFMAN. The Institute supports research designed to be of assistance to school systems in providing education for handicapped children. Emphasis is on research concerned with interventions, psychological and educational, with high risk infants and children under five. The objective is to bring children with early detected developmental delay and handicapping conditions to school age better prepared to move forward within the provisions of customary school and community resources. The Institute, however, does not provide direct consultation to school systems on educational matters. It does assist in the support of conferences designed to bring research information to professionals in the education community; and answers to questions posed by school personnel are provided on request. The Institute supports research concerned with hyperactivity in children and would like to be able to expand these efforts; it does not, however, have studies underway which measure the effects of handicapped and hyperactive children on regular classroom functioning.

MENTAL RETARDATION

Mr. CONTE. How well can we tell whether a child is mentally retarded or has some kind of communication disorder that can be confused with retardation?

Dr. CORFMAN. Present day diagnostic capabilities of our Nation's better diagnostic and evaluation centers provide, in the vast majority of cases, an accurate diagnosis which distinguishes mental retardation from pure communication disorders. These centers are customarily staffed by representatives of the several major disciplines concerned with the diagnosis and remediation of developmental disorders; and they possess the knowledge and skills required for comprehensive evaluation. Confusion in diagnosis of mental retardation with communication disorders and autism is prevalent in this country. Much of this confusion is consequent to unidisciplinary diagnosis from a professional bias, inadequate evaluation, or inadequately trained diagnosticians.

Mr. CONTE. Are any experiments in care of the retarded being carried out abroad that we can learn from?

Dr. CORFMAN. An Israeli investigator under NICHD support has developed highly innovative diagnostic instruments and materials which predict and enhance intellectual skills in children and youth from socio-culturally deprived backgrounds who are educationally and functionally mentally retarded. Although modification or reversal of intellectual performance in adolescence, especially among those living in residential facilities, is usually considered unlikely, individuals in this project have shown significant improvement in the learning process, social integration, self-acceptance and level of functioning. The instrumental enrichment technique utilizes specifically designed exercises to remediate specific, diagnostically determined impaired functions. These methods are being widely and successfully applied through the Israeli public school system and are beginning to be experimentally applied in various parts of the United States.

AGING

Mr. Conte. The aging program is the smallest of the Institute's major program interests, and has an actual decrease in 1975. Short of creating a new Institute on aging, how can we get more attention paid to this field?

Dr. Corfman. Although the aging research program is the smallest of the Institute's program, it is still substantial in size and has almost doubled in the past 5 years, from $8 million in 1970 to $15.6 in 1974. Further, even though the estimate for 1975 shows a reduction in obligations, the actual program level shows an increase of approximately $100,000 in 1975. We feel that we have achieved the best possible balance between our three program responsibilities—aging, population, child health—within our available resources. The funding rates are approximately the same for these three programs; and any change in emphasis in one program would impinge on the resources available for our other important research efforts.

Any increase in the Institute's budget would dictate a reevaluation of this program balance.

Mr. Conte. Has any of the Institute's work on aging had direct implications for service programs?

Dr. Corfman. A study carried out by one investigator concerned personality characteristics of individuals in nursing homes and homes for the aging. Environmental settings and characteristics of these homes were also studied in an attempt to match personality characteristics of patients with environments of the homes. This study provides important information for the establishment of different types of homes for the aging in order to best meet their needs.

Two other studies pointed out the detrimental effects of moving elderly people from living environments to which they had become accustomed. Moving elderly people from their homes to institutions, or from one institution to another, imposed severe strain on the elderly, which resulted in increased morbidity and mortality.

It has been reported by an investigator conducting research on an elderly population, that it is of importance to elderly people that they maintain social relationships with others. Those that maintained social contacts were found to be more healthy and better adjusted than those who did not.

SUDDEN INFANT DEATH SYNDROME

Mr. Robinson. We acknowledge the crushing emotional impact on parents when a child suffers the sudden infant death syndrome. Do the investigations suggest that the prime cause is a neurological deficiency, or can it perhaps be a heart deficiency?

Dr. CORFMAN. It is not felt that the primary cause of SIDS is either a "neurological deficiency" nor a "heart deficiency." However, several investigators have demonstrated an immaturity of breathing receptors in certain infants. Others have demonstrated the cessation of breathing (apnea) during various stages of sleep. These responses support the hypothesis that immaturity of certain brain centers, as well as peripheral receptors, may be involved in sudden infant death syndrome.

A phenomen associated with apnea is a lowering of oxygen transport to the tissues. When tissue oxygen levels reach certain low levels, changes in their function occur. The heart is a very sensitive organ to lowered tissue oxygen. Often cardiac arrythmias, which may be fatal, ensue. Thus, investigators have formulated the working hypothesis that apnea, usually associated with sleep, lowers tissue oxygen. This low oxygen causes malfunction and disordered rate and rhythm of the heart, which may cause sudden death.

ADOLESCENCE

Mr. ROBINSON. You mention that in the past year, you have launched an expanded program on adolescent development, and that very little is known about either the biological or behavioral aspects of this stage of a person's life. What are the objectives of this expanded program in terms of solving known problems?

Dr. CORFMAN. In the past, a great deal more research emphasis has been placed on very early and very late development than on adolescence. Yet, the teenage years constitute a critical period of development, a period of profound biological and psychological change. It is a period of special difficulties for many young people and their families in our country today. We realize the great need for further research on these problems. I would be pleased to provide more detailed information for the record.

[The information follows:]

NICHD'S PROGRAM ON ADOLESCENT DEVELOPMENT

Following is a description of the NICHD's program on adolescent development. The NICHD realizes the great need for research on adolescent development, and has identified five areas of particular research interest. A great deal of research is needed in each of these areas, but following are examples of how our research may contribute to the solution of a few known problems.

(1) *Biological processes involved in the onset and completion of puberty.*—One of the specific goals is to discover the cause of delayed puberty, a source of great anxiety and stress to the teenager and his or her parents. Presently, little is known of the exact mechanism which triggers pubertal onset; but certain parts of the brain have been implicated, especially the hippocampus and the hypothalamus. Somewhere in this brain tissue lies a biological clock sensitive to timed events in nature. Once the operation of this clock is established, physicians may be able to advance its timing in cases where the onset of puberty has gone awry.

(2) *Nutritional needs of teenagers.*—In our country today, an increasing proportion of infants are born to young teenage mothers, and the neonatal mortality rate for mothers under 15 years of age is roughly twice that for mothers 20 to 24 years of age. There is concern that the extra nutritional demands of pregnancy, superimposed upon adolescent growth requirements, may cause stress resulting in low-birth-weight infants and increased neonatal mortality. Longitudinal research studies are needed to define the physiological, nutritional, and psychological effects of early pregnancy on both mother and infant. Significant numbers of adolescents also suffer from obesity, and it is well known that the individual who becomes obese during childhood or adolescence will usually remain obese during adulthood. Impaired physical and mental health, as well as reduced

longevity, are correlates of obesity. Effective programs for the prevention and treatment of obesity apparently depend on a better understanding of the basic mechanism of metabolism and appetite regulation during the adolescent growth spurt, when a high proportion of individuals show the onset of obesity. Through the adolescence research program, the NICHD hopes to support research which will provide answers to some of these important questions.

(3) *Intellectual development of teenagers.*—The language and thought processes typical of this age, and how these processes interact with the development of motivation and attitudes, are of extreme importance. For example, we would like to know how intellectual processes relate to motivational processes in academic achievement or a lack of interest in schools.

Many of our schools report a high dropout rate for teenagers. We would like to know how the development of intellect and attitudes may interact in the determination of academic achievement or failure.

(4) *Adolescent socialization.*—One priority in this area is to discover how social structures, including the family, influence the teenager to choose appropriate or inappropriate adult roles. One of the fundamental human motives is the maintenance and enhancement of the self, and it is during adolescence that the individual forms many critical aspects of his self concept ("ego identity"). A greater knowledge of this area will help us understand how the adolescent behaves, how he chooses his friends, relates to his parents, chooses his opinions and values, and whether he engages in delinquent or socially useful behavior.

(5) *The relationship between changing hormonal levels and personality development during adolescence.*—We know that rapid and marked changes occur in the levels of circulating hormones during adolescence, and that other biological events with important psychological implications occur during this period (for example, the beginning of menstruation in girls). We would like to determine how these two different kinds of events relate to each other during this period of rapid development. This may help us determine, for example, how a teenager comes to establish an adequate definition of his appropriate adult sex role.

CONTRACEPTIVE PILL

Mr. Robinson. I understand that one of the growth hormones diethylstilbestrol (DES) is used as a morning-after contraceptive pill. This is permitted by FDA. However, this same compound is absolutely prohibited from use as an implant in beef animals to stimulate additional growth because it is known to be carcinogenic when used in very high dosages. Have you done any research in this area, and if so, would you comment upon it?

Dr. Corfman. We have not supported any research on the use of diethylstilbestrol as a morning-after contraceptive pill, although we have examined the results of studies in which DES was used for this purpose. These studies indicate that large doses of the drug, administered for 5 days beginning within 24 hours of exposure, will prevent pregnancy. If pregnancy should occur after such doses, there is concern for its effects on female offspring as they mature. In view of the suspicion that the use of this compound during pregnancy may cause vaginal cancer in female offspring, we are this year supporting a study of the children of women who took DES 20 years ago as a method of avoiding miscarriages and other complications of pregnancy.

Mr. Flood. Thank you.

NATIONAL INSTITUTES OF HEALTH

National Institute of Child Health and Human Development

Amounts Available for Obligation [1/]

	1974 Revised	1975
Appropriation	$130,254,000	$124,897,000
Amount withheld (PL 93-192)	5,357,000	---
Subtotal, adjusted appropriation	124,897,000	124,897,000
Real transfer to:		
"Departmental Management" (For Department-wide reductions in public affairs)	-30,000	---
Comparative transfers to:		
"Office of the Assistant Secretary for Health" (Transfer of administrative support activities to the Office of the Assistant Secretary for Health)	-73,000	---
"Departmental Management" (Transfer of accounting functions from the OS Working Capital Fund)	-7,000	---
Comparative transfers from:		
"National Institute of General Medical Science" (Decentralization of scientific evaluation grants program)	+155,000	---
"Departmental Management" (Transfer of indirect cost negotiation function to the OS Working Capital Fund)	+8,000	---
Subtotal, budget authority (base obligations)	124,950,000	124,897,000
Unobligated balance, restored	19,243,000	---
Comparative transfer of restored unobligated balance to Research Resources for General Research Support Grants	-2,950,000	---
Total, obligations	141,243,000	124,897,000

[1/] Excludes the following amounts for reimbursable activities carried out by this account: 1974 - $45,000; 1975 - $45,000.

Summary of Changes

1974 Estimated obligations	$141,243,000
1975 Estimated obligations	124,897,000
Net change	-16,346,000

	1974		Change from 1974	
	Pos.	Amount	Pos.	Amount
Increases:				
A. Built-in:				
1. Annualization of 1974 pay increase cost	--	---	--	+$168,000
2. Within-grade pay increases	--	---	--	+265,000
3. Extra day of pay in 1975	--	---	--	+34,000
4. FTS rate increase	--	---	--	+30,000
5. Bureau of Employee Compensation	--	---	--	+5,000
6. Service and supply fund increase	--	---	--	+25,000
7. Gerontology Research Center maintenance contract	--	---	--	+20,000
Subtotal	--	---	--	+547,000
B. Program:				
1. Research grants:				
a. Noncompeting continuations	--	$40,186,000	--	+21,496,000
b. Competing (new, continuations, and supplementals)	--	---	--	+13,621,000
c. Special programs	--	8,434,000	--	+27,000
2. Fellowships:				
a. Noncompeting continuations	--	280,000	--	+2,570,000
b. Competing (new)	--	---	--	+2,065,000
3. Training grants - noncompeting	--	6,693,000	--	+2,400,000
4. Intramural, laboratory and clinical research	338	11,265,000	+10	+300,000
Subtotal	--	---	+10	+42,479,000
Total, increases	--	---	+10	+43,026,000
Decreases:				
A. Built-in:				
1. Payment to "National Institutes of Health Management Fund"	--	---	--	-138,000

Summary of Changes - Continued

B. Program:				
1. Research grants:				
a. Noncompeting completed or converted to competing status............	--	$40,186,000	--	$-13,261,000
b. Competing completed or converted to noncompeting......	--	---	--	-28,294,000
c. 1974 obligations used to fund 1975 continuations.....	--	---	--	-6,438,000
d. Special programs....	--	8,434,000	--	-757,000
2. Fellowships:				
a. Noncompeting completed or converted to competing status............	--	280,000	--	-234,000
b. Competing completed or converted to noncompeting......	--	---	--	-2,816,000
c. 1974 obligations used to fund 1975 continuations.....	--	---	--	-281,000
3. Training grants:				
a. Noncompeting completed or converted to competing status............	--	6,693,000	--	-2,100,000
b. Competing completed or converted to noncompeting......	--	---	--	-3,362,000
c. 1974 obligations used to fund 1975 continuations.....	--	---	--	-962,000
4. Research and development contracts.............	--	20,947,000	--	-729,000
Subtotal.......	--	---	--	-59,234,000
Total, decreases....	--	---	--	-59,372,000
Total, net change...........	--	---	+10	-16,346,000

Explanation of Changes

Increases:

A. Built-in: These increases will provide: $168,000 for annualization of the 1974 pay increase cost, $265,000 for within-grade pay increases in 1975, $34,000 for extra day of pay in 1975, $30,000 for increased costs in 1975 of using the Federal Telecommunications System, $5,000 for Bureau of Employee Compensation, $25,000 for increased rates in the service and supply fund in 1975, and $20,000 for increased rates in the Gerontology Research Center maintenance contract.

B. Program:

1. Research grants:

a. The increase of $21,496,000 in noncompeting regular research grants represents the increased cost for continuation of previously awarded grants plus 333 "new" continuations resulting from grants made in 1974. The total number of noncompeting regular research grants will increase by 137 from 608 in 1974 to 745 in 1975.

b. The amount of $13,621,000 in competing regular research grants reflects: (a) $8,660,000 for 140 new awards; (b) $4,621,000 for 55 competing continuations; and (c) $340,000 for supplementals.

c. The increase of $27,000 in special programs represents increased cost of scientific evaluation grants.

2. Fellowships:

a. The increase of $2,570,000 in noncompeting fellowships represents the increased cost for continuation of previously awarded fellowships plus 191 "new" continuations resulting from fellowships made in 1974. The total number of noncompeting fellowships will increase by 174 from 20 in 1974 to 194 in 1975.

b. The amount of $2,065,000 in competing fellowships will support 153 new fellowships in 1975.

3. Training grants - The increase of $2,400,000 in noncompeting training grants represents the increased cost for continuation of previously awarded training grants plus 20 "new" continuations resulting from training grants made in 1974. The total number of noncompeting training grants will increase by 20 from 60 in 1974 to 80 in 1975.

4. Intramural, laboratory and clinical research - The increase of 10 positions and $300,000 will provide for an expansion of the research program in perinatal biology.

Decreases:

A. Built-in: The decrease of $138,000 in payment to the NIH Management Fund represents a decrease in this Institute's proportionate share of the cost for centrally furnished services.

B. Program:

1. Research grants:

a. The decrease of $13,261,000 represents 196 noncompeting regular research grants that were completed in 1974 or that are being converted to competing status in 1975.

Explanation of Changes - Continued

b. The decrease of $28,294,000 consists of $21,856,000 which reflects the completion or conversion to a noncompeting status of 340 competing grants and $6,438,000 for the first year cost of 104 two-year grants awarded in 1974.

c. The decrease of $6,438,000 reflects the reduced funding required in 1975 due to the two-year funding of 104 projects in 1974.

d. The decrease of $757,000 in special programs represents a decrease of 19 research career development awards in 1975.

2. Fellowships:

a. The decrease of $234,000 represents 17 noncompeting fellowships that were completed in 1974.

b. The decrease of $2,816,000 consists of $2,535,000 which reflects the completion or conversion to a noncompeting status of 197 competing fellowships and $281,000 for the first year cost of 27 two-year fellowships awarded in 1974.

c. The decrease of $281,000 reflects the reduced funding required in 1975 due to the two-year funding of 27 fellowships in 1974.

3. Training grants:

a. The decrease of $2,100,000 represents the phase-out of this program after the training under previously approved training grants is completed.

b. The decrease of $3,362,000 consists of $2,400,000 which reflects the completion or conversion to noncompeting status of 20 competing training grants and $962,000 for the first year cost of 13 two-year training grants awarded in 1974.

c. The decrease of $962,000 reflects the reduced funding required in 1975 due to the two-year funding of 13 projects in 1975.

4. Research and development contracts - The decrease of $729,000 will result in a reduction of effort in the population and child health research contract programs.

Obligations by Activity

Page Ref.		1974 Base *		1975 Estimate		Increase or Decrease	
		Pos.	Amount	Pos.	Amount	Pos.	Amount
52	Population.............	--	$39,438,000 (45,927,000)	--	$40,282,000	--	+$844,000[A]
58	Child health...........	--	51,992,000 (60,342,000)	--	52,278,000	--	+286,000[B]
71	Aging..................	--	10,970,000 (12,424,000)	--	9,078,000	--	-1,892,000[C]
75	Intramural, laboratory and clinical research.	338	14,225,000	348	14,727,000	+10	+502,000[D]
80	Research management and program services..	181	8,325,000	181	8,532,000	--	+207,000[E]
	Total obligations (bases)...............	519	124,950,000	529	124,897,000	+10	-53,000
	Total obligations.......		(141,243,000)				

Explanation of Changes (by Activities)

A) Population - The increase of $844,000 in population research will provide for increased efforts in contraceptive development and evaluation and behavioral sciences.

B) Child health - The increase of $286,000 in child health research will provide for increased efforts in perinatal biology and infant mortality, mental retardation and adolescence.

C) Aging - Although the aging program is decreasing by $1,892,000 in 1975, the program level is approximately the same as 1974, because a substantial portion of the 1974 research grant funds was used to support two-year awards.

D) Intramural, laboratory and clinical research - The increase of 10 positions and $502,000 in intramural, laboratory and clinical research includes $339,000 for mandatory increases, and a program increase of 10 positions and $300,000, which will provide for an expansion of the research program in perinatal biology, offset by a decrease of $137,000 in the NIH Management Fund for centrally furnished services.

E) Research management and program services - The increase of $207,000 in research management and program services includes $208,000 for mandatory increases, offset by a decrease of $1,000 in the NIH Management Fund for centrally furnished services.

* 1974 Base - Excludes 1973 appropriation restorations. Total obligations shown in parentheses.

Obligations by Object

	1974 Estimate	1975 Estimate	Increase or Decrease
Total number of permanent positions..	519	529	+10
Full-time equivalent of all other positions.........................	84	84	--
Average number of all employees......	602	608	+6
Personnel compensation:			
Permanent positions...............	$8,812,000	$9,328,000	+$516,000
Positions other than permanent.....	825,000	840,000	+15,000
Other personnel compensation.......	167,000	180,000	+13,000
Subtotal, personnel compensation.	9,804,000	10,348,000	+544,000
Personnel benefits..................	1,081,000	1,130,000	+49,000
Travel and transportation of persons.	385,000	395,000	+10,000
Transportation of things............	86,000	95,000	+9,000
Rent, communications, and utilities..	516,000	400,000	-116,000
Printing and reproduction...........	145,000	150,000	+5,000
Other services:			
Project contracts.................	20,947,000	20,218,000	-729,000
Payment to NIH management fund.....	4,681,000	4,543,000	-138,000
Other..............................	3,667,000	3,949,000	+282,000
Supplies and materials..............	1,410,000	1,499,000	+89,000
Equipment...........................	775,000	750,000	-25,000
Grants, subsidies, & contributions...	97,746,000	81,420,000	-16,326,000
Total obligations by object........	141,243,000	124,897,000	-16,346,000
Total obligations excluding 1973 appropriation..............	124,950,000		

Significant Items in House and Senate Appropriations Committee Reports

Item	Action taken or to be taken
1974 House Report	
1. The Committee was concerned with the priority of aging research in the Institute and directed that a substantial portion of the Congressional increase be used for this purpose. (Page 41)	1. The Institute continues to stress aging research. In 1974, the Institute will spend approximately $15,586,000, an increase of $2,937,000 over the 1973 level.
1974 Senate Report	
1. The Committee expressed concern over the level of effort in research on the sudden infant death syndrome (SIDS). (Page 54)	1. The level of support for research on the sudden infant death syndrome is $4,700,000 in 1974, an increase of $600,000 over the 1973 level.
2. The Committee expressed concern that too little research bearing on adolescent development was being conducted and recommended that this research area be vigorously pursued. (Page 55)	2. The Institute has expanded its program of research on adolescent development; the program has increased from a level of $1,100,000 in 1973 to $1,500,000 in 1974.
3. The Committee recommended that research into all aspects of population problems should be featured and emphasized. (Page 55)	3. In 1974, the Institute will spend approximately $44,858,000 on population research, an increase of $5,007,000 over the 1973 level.
4. The Committee considered that the aging research effort should be afforded one of the highest priorities in the health field. The Committee directed that a significant portion of the increase be used to give aging research increased and special emphasis. (Page 56)	4. In 1974, the Institute will spend approximately $15,586,000 on aging research, an increase of $2,937,000 over the 1973 level.

Authorizing Legislation

Legislation	1975 Authorization	 Appropriation Requested
Public Health Service Act Section 301--Research and Investigation, in general............................	Indefinite	$124,897,000
Title IV, Part E--National Institute of Child Health and Human Development.......	Indefinite	

National Institute of Child Health and Human Development

Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
1965	$40,264,000	$40,791,000	$39,813,000	$39,813,000
1966	50,138,000	50,138,000	51,296,000	51,645,000
1967	57,415,000	57,615,000	61,115,000	61,115,000
1968	64,226,000	64,226,000	69,296,000	64,213,000
1969	71,312,000	66,777,000	72,277,000	69,044,500
1970	71,770,000	69,016,000	76,718,000	73,110,000
1971	89,844,000	89,977,000	89,977,000	89,977,000
1972	99,757,000	105,688,000	121,653,000	112,853,000
1973 *	109,604,000	126,002,000	155,573,000	126,002,000 *
1974	106,732,000	125,307,000	135,307,000	130,307,000 **
1975	124,897,000			

* Note: This appropriation authority was the continuing resolution. The appropriation amount was the House Allowance, which was the lower of the House or Senate amounts in the first vetoed bill.

** Appropriation after reduction, $124,950,000.

Justification

National Institute of Child Health and Human Development

	1974 Base *		1975 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits..............	519	$10,885,000	529	$11,478,000	+10	+$593,000
Other expenses..............	--	114,065,000	--	113,419,000	--	-646,000
Total................	519	124,950,000	529	124,897,000	+10	-53,000

General Statement

The public, as well as the scientific community, has recognized the need for the study of man during the entire life span, for investigations and inquiries that will reveal, with sharp definition, the normal development and potentialities of the human individual. Life span research means a pattern of study concerned with the interrelatedness of the different periods of human development. The National Institute of Child Health and Human Development is the only research organization in the country whose mission is dedicated to the study of developmental processes pertaining to any point of the human life span. The goals are to improve the quality of life, to reduce morbidity and mortality, and to increase man's ability to cope with his environment. All aspects of human development, physical, psychological, and social, and their relationships to health must be actively examined. The interdependence of various kinds of development is stressed as well as the significance of each stage of development in relation to subsequent ones.

The population program supports research aimed at developing and improving contraceptive methods for use by couples wishing to space and limit their families and the investigation of the many behavioral and social aspects of population problems in an effort to understand the dynamics of family planning behavior. Research such as this, combined with family planning services offered by Federal and other agencies, will afford every individual the opportunity to have the number of children he or she desires. The population research effort is necessary for evolution of policies and development of technology for dealing with population-related problems.

The child health program fosters and conducts research on human development from the moment of conception through adolescence to adulthood. This focus includes the health of the mother; the effect of her health on the child both before and after birth; and the intact survival or well-being of the child through the hazards of intrauterine life, the birth process, and the adjustments to the new environment. The Institute's focus then shifts to the study of nutritional, genetic, social, psychological, and other factors relating to the kind of person the infant will become. Research encompasses normal development of children and youth, abnormal development and mental re-

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* Excludes 1973 appropriation restorations.

tardation, and infant survival and well-being.

Ten percent of the U.S. population is older than 65 years, and 80 percent of those over 65 have at least one serious disability. Moreover, the Census Bureau predicts that within the next 50 years, the number of persons in the United States over 65 will double to 40 million. Two-thirds of the Federal money spent on health care in this country is spent on persons over 65. One million persons over 65 live in institutions and a significant portion of these are incapacitated by senile dementias. The aim of the research program on aging is to make it possible for these older persons to enjoy good health and remain participating members of society. The degenerative aging processes that begin early in life and whose results surface as disabilities in middle and late life must be studied and understood in such depth that they can be abolished, slowed, or compensated for.

To show a complete view of the Institute's three major program areas, the following table identifies total funding estimates by program area, each including the associated Intramural, Laboratory and Clinical Research funding and a proportionate share of the Research Management and Program Services activity, exclusive of the funds for the NIH Management Fund.

	1974 Base *	1975 Estimate	Increase or Decrease
Population..................	$44,858,000	$45,874,000	+$1,016,000
Child health................	59,825,000	60,625,000	+800,000
Aging.......................	15,586,000	13,855,000	-1,731,000

* Excludes 1973 appropriation restorations.

DHEW - National Institutes of Health

CROSSWALK - 1974 COLUMN 1975 PRESIDENT'S BUDGET

INSTITUTE: National Institute of Child Health and Human Development
(In thousands)

Mechanism / Program	Research Grants						Laboratory and Clinical Research	Research and Development Contracts	Other Direct Operations	Total
	Regular Program		Specials		Training Programs					
	Non-competing	Competing	Multi-disciplinary Centers	Other	Grants	Fellowships				
1974 Base Obligations										
1. Population..............	$13,074	$ 9,743		$ 809	$1,117	$ 726		$13,969		$39,438
2. Child health............	22,212	12,600	$5,608	1,792	4,071	1,645		4,064		51,992
3. Aging...................	4,900	3,759		139	1,136	371		665		10,970
4. Intramural, laboratory and clinical research.							$13,519		$ 706	14,225
5. Research management and program services......									8,325	8,325
Subtotal..............	40,186	26,102	5,608	2,740	6,324	2,742	13,519	18,698	9,031	124,950
Unobligated Balance Restored										
1. Population..............		3,200		61	1,250	388		1,590		6,489
2. Child health............		4,835		25	2,718	213		559		8,350
3. Aging...................		595			725	34		100		1,454
Subtotal..............		8,630		86	4,693	635		2,249		16,293
Total Obligations..........	40,186	34,732	5,608	2,826	11,017	3,377	13,519	20,947	9,031	141,243

DHEW - National Institutes of Health

CROSSWALK - 1975 COLUMN 1975 PRESIDENT'S BUDGET

INSTITUTE: National Institute of Child Health and Human Development
(In thousands)

Mechanism	Research Grants									
			Specials							
	Regular Program		Multi-disciplinary		Training Programs		Laboratory and Clinical	Research and Development	Other Direct	
Program	Non-competing	Competing	Centers	Other	Grants	Fellowships	Research	Contracts	Operations	Total
1. Population..............	$15,629	$5,234		$ 706	$1,957	$1,588		$15,168		$40,282
2. Child health............	28,242	6,571	$5,608	1,295	3,880	2,432		4,250		52,278
3. Aging...................	4,550	1,816		95	1,156	661		800		9,078
4. Intramural, laboratory and clinical research.							$14,012		$ 715	14,727
5. Research management and program services......									8,532	8,532
Total Obligations..........	48,421	13,621	5,608	2,096	6,993	4,681	14,012	20,218	9,247	124,897

National Institute of Child Health and Human Development

Budget Mechanism

	1974 *		1975	
	Number	Amount	Number	Amount
Grants				
Regular				
Non-competing............	608	$40,186,000	745	$48,421,000
Competing................	85	8,104,000	55	4,621,000
New......................	221	17,658,000	140	8,660,000
Supplemental.............	(20)	340,000	(20)	340,000
Subtotal..............	914	66,288,000	940	62,042,000
Special				
Mental retardation research centers.......	12	5,608,000	12	5,608,000
Research career programs...............	90	2,585,000	74	1,914,000
Scientific evaluation....	--	155,000	--	182,000
Subtotal..............	102	8,348,000	86	7,704,000
Total research grants......	1,016	74,636,000	1,026	69,746,000
Fellowships				
Non-competing.............	20	280,000	194	2,616,000
Competing.................	1	18,000	--	---
New.......................	155	2,444,000	153	2,065,000
Supplemental..............	--	---	--	---
Subtotal................	176	2,742,000	347	4,681,000
Training grants				
Non-competing.............	60	4,400,000	80	6,993,000
Competing.................	10	1,540,000	--	---
New.......................	3	384,000	--	---
Supplemental..............	--	---	--	---
Subtotal................	73	6,324,000	80	6,993,000
Intramural, laboratory & clinical research:				
Laboratory & clinical research.................	--	13,519,000	--	14,012,000
Biometry, epidemiology & field studies...........	--	706,000	--	715,000
Research & development contracts.................	--	18,698,000	--	20,218,000
Research management & program services..........	--	8,325,000	--	8,532,000
Total.....................	--	124,950,000	--	124,897,000

* Excludes 1973 appropriation restorations.

Population

Authorizing Legislation: Public Health Service Act, Title IV, Part E

	1974 Base *		1975 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits...........	---	---	---	---	---	---
Other expenses..........	---	$39,438,000	---	$40,282,000	---	+$844,000
Total..........	---	39,438,000	---	40,282,000	---	+844,000
Subactivities:						
Contraceptive Development.................	---	6,569,000	---	7,068,000	---	+499,000
Contraceptive Evaluation.................	---	4,100,000	---	4,500,000	---	+400,000
Directed Behavioral Research.............	---	3,300,000	---	3,600,000	---	+300,000
Research Fundamental to the Population Sciences............	---	25,469,000	---	25,114,000	---	-355,000
Total..........	---	39,438,000	---	40,282,000	---	+844,000
Budget Mechanism:						
Research Grants:						
Regular.............	---	22,817,000	---	20,863,000	---	-1,954,000
Special.............	---	809,000	---	706,000	---	-103,000
Subtotal..........	---	23,626,000	---	21,569,000	---	-2,057,000
Fellowships...........	---	726,000	---	1,588,000	---	+862,000
Training Grants........	---	1,117,000	---	1,957,000	---	+840,000
Research and Development Contracts.......	---	13,969,000	---	15,168,000	---	+1,199,000
Total..........	---	39,438,000	---	40,282,000	---	+844,000

Introduction:

The National Institute of Child Health and Human Development and its Center for Population Research (CPR) have the primary responsibility for the Federal effort in population research. The scope of the population and reproduction research program encompasses research on the development of new means of fertility regulation, the evaluation of contraceptive methods currently in use, and the analysis of social and behavioral factors in population growth, change and distribution. The program also includes the Institute's effort in fundamental

* Excludes 1973 appropriation restorations.

research in reproductive biology and the social sciences, upon which advances in contraceptive development and the solution to problems associated with population dynamics are dependent. In addition, an integral part of the Institute's population program is to support institutions, develop scientific manpower, and facilitate the coordination of Federal population research programs and the communication of research information in the population sciences. In all of these areas, there have been major accomplishments and continuing developments which promise to improve the safety and efficacy of contraception and to build a substantial research base for the formulation of effective population policy.

The population research program is accomplished through the award of research grants, including the Population Research Centers; fellowships; training grants; and research contracts; and the conduct of intramural research. The funds and description of programs for the intramural research effort are contained within the activity Intramural, Laboratory and Clinical Research. The funds to support the staff necessary to provide the scientific and administrative management of the population program are contained within the activity Research Management and Program Services.

Program Plans, 1975

Contraceptive Development - In 1975 further research will be directed to investigating immunological approaches to contraception. The concept of developing an immunity to sperm in the female, or a self-immunizing response to sperm in the male has been raised in the past. These concepts have not been tested adequately as the knowledge of how to cause the responses without serious untoward effects has been lacking. Recently developed knowledge of antigen-antibody formation and interaction now furnishes the basis for study of possible immunological approaches to contraception.

Little is known of biochemistry as affected by the hormonal control of many unique processes in reproduction. It is known, for example, that the process of fertilization is facilitated by one or more enzymes of sperm origin. However, such enzymes have not been fully studied. Efforts will be initiated utilizing appropriate disciplines to explore the potential of a biochemical basis for interference with fertilization.

Efforts will continue for development of a long-acting injectable contraceptive. Clinical and regulatory requirements for research in this area, which have delayed initiation of this program, will be resolved in 1975, and the research will be undertaken.

Contraceptive Evaluation - Continuation of projects initiated in previous years is expected to provide increasingly authoritative information on the medical effects of contraceptive and sterilization methods in use. Particular emphasis will be given to the adverse medical events and long term complications with vasectomy, an increasingly popular method of male sterilization. The established clinical and epidemiological surveillance is expected to identify the significance of potential health hazards of vasectomy.

Activity will be expanded in evaluation of oral contraceptives and high blood pressure. Also, additional studies will be initiated to examine the relationships between contraceptive practice and maternal and infant mortality and morbidity.

Directed Behavioral Research - New research efforts will differ from the current program which concentrates on social and economic changes affecting the birth rate. New investigations will be initiated to study the social and psychological factors which determine effective contraceptive practice. The strength of motivation for birth control and attitudes toward various methods will be studied with particular emphasis on male attitudes. Data from teenagers and young unmarried adults may provide valuable indicators for the acceptability and use of fertility control methods which are available or under development.

Research Fundamental to the Population Sciences - Efforts in the basic reproductive biology program will continue toward the development of fundamental biomedical research leads and the exploitation of these leads to obtain increased knowledge of fertility regulation and infertility problems.

A major focus of the fundamental biomedical research effort in population will continue to be located within the Population Centers program. A unique characteristic of population centers is their aggregate resource of scientists working on various aspects of population and reproductive phenomena. Increased emphasis will be given to this area so that coordinated, multidisciplinary endeavors in fundamental research can be increased. Special effort will be undertaken to stimulate cooperative research in population phenomena using social science and biomedical researchers as co-investigators.

The primary emphases of the biomedical program in population research are: 1) the development of safe, effective, inexpensive measures for fertility regulation that will be accepted and used by diverse population groups; and 2) the continued support of fundamental work on reproductive processes in humans and experimental animals. These efforts are indivisibly related. As in other sciences, breakthroughs in contraceptive development will stem from exploitation of critical masses of relevant scientific information. Such critical masses of information do not arise de novo but are the results of steady, sometimes slow, accretions of knowledge. Thus, fundamental biomedical research is the rate-limiting step in the development of satisfactory procedures for fertility regulation.

Several promising research leads will be followed up in 1975. The possibility of developing a contraceptive measure based on certain slightly modified hormone molecules will be investigated based on current and anticipated knowledge of the action of these hormones. Our understanding of the mechanism of action of the steroid hormones (progesterone in particular) reveals a wide variety of possibilities for interruption of this action, for potential contraceptive use.

Program Plans, 1974

Contraceptive Development - In the area of contraceptive development, the Institute is currently consolidating an expanding program of research aimed at new approaches to fertility regulation. Two of the three areas of endeavor, drug development and device development, offer the greatest promise of early tangible results. These areas plus the third, directed fundamental research in reproductive biology, represent efforts to balance pragmatic approaches to fertility regulation and the need for expanding the basic knowledge of reproductive processes to find new, safe and efficacious contraceptives for women, and to develop acceptable and effective contraceptives for men.

Synthesis of compounds related to prostaglandins (naturally occurring substances derived from fatty acids) seeks to separate their antifertility activity from undesired side effects. Some of these new compounds tested in the hamster show some separation of these two activities. In addition, a promising new drug, which is a modification of the female sex hormone (estrogen), has been shown to have high antifertility activity. This result was obtained in the rat and the drug is now being tested in other species including the monkey.

Concern over the use in the human of the artificial estrogen DES (diethylstilbestrol) as a postcoital contraceptive agent has led to the initiation of clinical studies on the safety and efficacy of other synthetic estrogens as well as natural estrogens of biologic origins. The aim of these studies is to determine whether these estrogens already on the market are safe.

Data from the testing of drugs as male contraceptive agents indicate that sperm production in the human can be drastically reduced through daily oral administration of a weak androgen (male hormone) combined with a once-a-month injection of a potent androgen. Acceptability of the method is good with a dropout rate of less than 10% and no reported effects on libido.

A number of new studies involve biodegradable materials, e.g., microcapsules containing the hormone progesterone can be injected with an ordinary syringe into cervical or muscle tissue to provide relatively constant drug release over 6-12 months. The polymer itself is digested by the tissue and is subsequently eliminated from the body. Biodegradable polymers capable of releasing a variety of antifertility drugs are being prepared.

Significant new knowledge of the basic physiology of the male reproductive tract is providing new ideas on possible ways of limiting male fertility without interfering with the other functions of the testis or with libido. Development and testing of devices intended for the achievement of easily reversible vasectomy have resulted in major advances. Some devices have been in laboratory animals more than 12 months and have been found to be effective. Preliminary data indicate that animals implanted with devices in the open position are fertile. The problem of the adhesion of the devices to body tissues has been resolved.

Contraceptive Evaluation - Current studies show that oral contraceptives do increase the risk of stroke. The frequency of such complications can be reduced by lowering the dosage of the drugs. Hypertension, regular cigarette smoking and a history of migraine increase the risk of stroke when combined with current use of oral contraceptives.

Analysis of the data on chromosome breakage in cultured blood cells from women taking oral contraceptives and control subjects has demonstrated a small but significant increase in breakage in cells from oral contraceptive users. Oral contraceptive agents also appear to alter the requirements for several vitamins and minerals. Several projects are underway to assess the scope and significance of these findings.

Progress has been made in defining the antigens (substances which produce body defense reactions) of sperm which may initiate an immune reaction after vasectomy. In a comprehensive two-year study of hormone levels in the blood of men before and after vasectomy, thus far no significant changes in the levels of the tested hormones have been detected. If these preliminary results are confirmed, one area of concern about possible adverse effects of vasectomy will have been eliminated.

Directed Behavioral Research - The goals of the behavioral sciences program of research in population continue to be 1) to ascertain the social, psychological, and economic determinants of fertility in the United States and 2) to develop an increased understanding of the consequences of population growth and change so that public policy may be guided by adequate information.

The relationship between the status of women, especially their employment status, and their fertility is receiving attention. Early labor force participation, type of work, career aspirations, social and psychological pressures, career selection, and job status are factors which appear to affect fertility decisions concerning the number and spacing of children.

The National Fertility Study of 1970 has shown that low income couples, probably through the efforts of family planning programs, have almost caught up to the level of contraceptive usage of high income couples.

When first enacted, legalization of abortion in California reduced the number of illegitimate births, but in the most recent year studied the rate of illegitimacy leveled off and then actually rose for white women under 20.

The Institute is also giving attention to the effect upon the birth rate of family planning programs, the reaction of ethnic groups to such programs, and the contraceptive effectiveness within such programs.

Research is being carried out on the effects of birth order, sex of infant, and socio-economic status of the mother-child-interaction. Another study will analyze data collected to evaluate the influence of family size and birth order on school and career achievement and fertility-related behavior, such as age at marriage, size of family, and birth spacing.

Research Fundamental to the Population Sciences - Of particular interest in fundamental research on the reproductive cycle is the production of the ovum (egg) and sperm for fertilization and conception (the taking in or implanting of the fertilized ovum in the uterus). Research is being conducted at all levels of the reproductive processes as modification or interruption of hormonal signals anywhere in the circuit could result in the prevention of conception.

Several important steps have been identified in the mechanism of action of progesterone and other sex steroids. Progesterone is often referred to as the hormone of pregnancy because its action on the uterus is required for the maintenance of pregnancy in the human as well as in other species. New knowledge in this area could form the basis for contraception through interdiction of progesterone action.

Several important observations have been made during the past year in the area of prostaglandin research which involve the possible role of these compounds in human ovulation, uterine contraction and the dissolution of the corpus luteum, a structure of the ovary necessary for early pregnancy maintenance.

In addition to the usual project grants and contracts, NICHD supports fundamental biomedical and behavioral population research conducted in Population Research Centers. The center concept provides for coordinated, interrelated progress in research on population problems on a broad front. Because of the possibilities for coordination of multidisciplinary efforts, fundamental research in population gains both a breadth and depth which offers the greatest opportunities for both discoveries and applications of those discoveries. Many of the most valuable research leads in fundamental population research have been produced in the Population Centers.

In 1974, three additional centers were opened, bringing the current total to ten in a planned network of twelve to fifteen.

Vanderbilt University
Nashville, Tennessee

University of Texas at Austin
Austin, Texas

Population Council at Rockefeller Univ.
New York, New York

University of Wisconsin
Madison, Wisconsin

University of Chicago
Chicago, Illinois

Harvard University
Cambridge, Massachusetts

Johns Hopkins University
Baltimore, Maryland

Baylor Medical College
Waco, Texas

University of North Carolina
Chapel Hill, North Carolina

Columbia University
New York, New York

Child Health

Authorizing Legislation: Public Health Service Act, Title IV, Part E

	1974 Base *		1975 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits.............	---	---	---	---	---	---
Other expenses.............	---	$51,992,000	---	$52,278,000	----	+$286,000
Total.............	---	51,992,000	---	52,278,000	---	+286,000
Subactivities:						
Perinatal Biology and Infant Mortality........	---	16,759,000	---	16,786,000	---	+27,000
Mental Retardation........	---	18,105,000	---	18,639,000	---	+534,000
Growth and Development....	---	17,128,000	---	16,853,000	---	-275,000
Total.............	---	51,992,000	---	52,278,000	---	+286,000
Budget Mechanism:						
Research Grants:						
Regular.................	---	34,812,000	---	34,813,000	---	+1,000
Special.................	---	7,400,000	---	6,903,000	---	-497,000
Mental Retardation Research Centers....	---	(5,608,000)	---	(5,608,000)	---	(---)
Subtotal.............	---	42,212,000	---	41,716,000	---	-496,000
Fellowships...............	---	1,645,000	---	2,432,000	---	+787,000
Training Grants...........	---	4,071,000	---	3,880,000	---	-191,000
Research and Development Contracts..............	---	4,064,000	---	4,250,000	---	+186,000
Total.............	---	51,992,000	---	52,278,000	---	+286,000

Introduction:

Biomedical and behavioral research endeavors that cover the life span from conception through the later teenage years define the Institute's Child Health Program. Research fields include the health of the mother; the effect of her health on the child both before and after birth; and the survival and well-being of the child through the hazards of intrauterine life, the birth process, and the adjustments to the new extrauterine environment. The focus then shifts to the study of nutritional, hormonal, genetic, social, psychological and other factors relating to the kind of adult the infant, child, and adolescent will become. Investigations include normal development of children and youth, abnormal development and mental retardation, and infant well-being and survival. This research is conducted within the three Child Health program areas: Perinatal Biology and Infant Mortality, Mental Retardation, and Growth and Development.

* Excludes 1973 appropriation restorations.

The child health research program is accomplished through the award of research grants, including Mental Retardation Research Centers; fellowships; training grants; and research and development contracts; and the conduct of intramural research. The funds and description of programs for the intramural research effort are contained within the activity Intramural, Laboratory and Clinical Research. The funds to support the staff necessary to provide the scientific and administrative management of the child health programs are contained within the activity Research Management and Program Services.

Perinatal Biology and Infant Mortality

The perinatal biology and infant mortality program is committed to the promotion of a coordinated research effort which will enhance understanding and development of knowledge as related to maternal health, pregnancy, embryonic development, fetal growth, and infant well-being through the first year of life. Research activities are also directed toward ameliorating infant morbidity, preventing infant death, and narrowing the gap between the identification of new knowledge and its incorporation into health care delivery.

In 1971, this nation's infant mortality rate was 19.2 per 1,000 live births, accounting for the death of approximately 68,200 infants before they had reached their first birthday. Approximately 75 percent of these babies (50,880) died during their first month of life; in more than half, death occurred during the first week of life. Despite an improvement in this country's infant mortality rate from 23.7 per 1,000 live births in 1966 to 19.2 in 1971, the United States' relative international ranking remained essentially unchanged: thirteen other developed countries reported more favorable rates. Nevertheless, encouragement can be derived from statistical indicators that demonstrate that this program's objectives and achievements have not been in vain. The decline in mortality rates is more significant when one considers that the average annual decline of less than one percent between 1950 and 1965 can now be compared to an average annual decline of 3.6 percent between 1969 and 1972.

Program Plans, 1975

It is now well known that infant morbidity and mortality can be increased by maternal disease and complications of pregnancy such as poor nutritional status, diabetes, high blood pressure, anemia, drug addiction, smoking, and the psychic stress of pregnancy. Scientific opportunities and expectations are encouraging for the health of the mother, child, and society. Future research will continue to probe mechanisms and seek to prevent these complications.

The most important single factor linked to our country's high infant death rate is low birth weight. While approximately 8 percent of all live births in the United States weigh less than 5.5 pounds, more than 70 percent of neonatal deaths occur among these low birth weight infants. Although there are many factors that contribute to low birth weight, prematurity (and the factors that cause prematurity) accounts for two-thirds of all low birth weight infants. Studies testing various hypotheses as to the controls on the duration of gestation and the events leading to the initiation of labor can offer leads to the solution of this problem. Efforts toward solving specific suspected causes and approaches to the prevention of low birth weight will be mounted. Further studies examining the epidemiology of intrauterine growth retardation must be pursued to enable identification of pregnancies at risk of producing low birth weight infants. Intrauterine infectious diseases and other noxious environmental substances at various periods during pregnancy require continued scientific research.

Research regarding the nature and causes of genetic problems as well as the ethics and efficacy of possible genetic counseling and manipulation warrants continued support.

Prenatal diagnosis and treatment are essential parts of the research efforts because many prenatal conditions and diseases, such as diabetes, contribute significantly to infant morbidity and mortality.

Efforts will also continue to understand the interplay of factors which determine the initiation of labor. Such information is necessary in order to insure optimal fetal development and retard premature labor. In conjunction with this, research will continue with the development of a fetal risk index so that the risk state of the fetus at any time in labor can be assessed and corrective or preventive measures be applied as warranted. The extension of previously completed research directed toward diagnostic procedures for monitoring the process of birth will be undertaken so that the prevention of aberrant states may be fully realized.

It is estimated that 2.5 to 3 infants per 1,000 live births succumb to the sudden infant death syndrome (SIDS). This equates to 7,500 to 10,000 infant deaths annually. The syndrome is the primary cause of death for those between the ages of one and twelve months. New leads have evolved that indicate that SIDS could be related to: heart rate changes, apnea, and infection; lack of sleep; oxygen deficiency; abnormality in the brain stem; immaturity of the nervous mechanism controlling heart function; and inadequate lung responses. Research is necessary to fully explore these new leads if the SIDS mystery is to be identified and combated. Specific avenues to be explored in 1975 include the distribution of SIDS within the population and characteristics surrounding its occurrence; identification of infants at high risk; studies of the structural and functional changes in tissues and organs which may be involved in SIDS; and the psychological stresses experienced by the family and the community in which SIDS occurs.

An important part of the SIDS endeavor is to inform the professional and lay communities about the problem and the approaches that are being taken to identify the underlying mechanism. The scientific information endeavor, consisting basically of workshops and publications, will be continued. It is a multifaceted effort that must encourage scientists to pursue research as well as to educate members of society - physicians, nurses, clergy, friends and families of SIDS victims, rescue workers, and others - to understand the problem and not show hostility toward the bereaved family.

Another major research area focuses on the psychosocial dynamics of pregnancy. In contrast to the relative wealth of information available concerning the biological aspects of pregnancy and pregnancy outcome, there is a paucity of knowledge about the relationship of attitudes and behavior of parents and grandparents to pregnancy outcome. Questions about the relevancy to pregnancy outcome of parental feelings of emotional and economic security, including feelings about self-worth, will be explored. Available information in this area is largely anecdotal and retrospective. A new effort will be directed toward identifying psychosocial factors operative during pregnancy, delivery, and the immediate post partum period which affect the fetus and newborn and which would contribute to infant morbidity and mortality. Basically these include: 1) maternal and paternal attitudes and behavior during pregnancy and throughout the first month of the infant's life, and 2) the impact of maternal stress, fears, and conflicts on the physiology of pregnancy.

Program Plans, 1974

Research into the causes of maternal disease and complications such as poor nutritional status, diabetes, high blood pressure, anemia, drug use, and other health problems is being enriched.

A variety of drugs currently in common use are producing congenital malformations when they are taken in the early months of pregnancy. Studies so far show that these malformations consist of defects or combinations of defects which are indistinguishable from spontaneously occurring malformations for which the incidence is already relatively high.

Significant new knowledge has emerged in the past year regarding low birth weight infants, a group with concentrated morbidity and mortality. Both premature infants and those of low birth weight for gestational age have benefited from studies in detection of fetal maturity in utero, induction of pulmonary maturation, recognition of fetal and neonatal growth retardation, and congenital and acquired infectious processes. Additional studies on genetic factors in low birth weight infants are on-going. Clinical advances in the recognition and treatment of jaundice, respiratory distress syndrome, thermal regulation, chemical adaptation and infection in the newborn have resulted from recent investigations. These findings are helping to save many infant lives.

Studies currently in progress include areas such as: prenatal diagnosis and treatment of a variety of conditions and diseases such as infections and diabetes; fetal-placental steroid hormone relationships; fetal hypothalamic structures; maternal uterine receptors; and electro-physiological properties of the uterus during gestation, at the initiation of labor and during birth. Non-premature, low birth weight infant situations are under intense investigation. One study nearing completion is showing that calorie supplementation, a high protein diet, and avoidance of certain medications during pregnancy can counteract many of the problems of low birth weight and malnutrition of newborns.

The greatest number of perinatal deaths occur within the 24 hours before birth and the 24 hours after birth. Approximately 10,000 fetal deaths occur after admission of the mother to the hospital in anticipation of a normal birth. In addition, 50 percent of all neonatal deaths happen before the infants are 24 hours old. Alterations in the normal processes in labor, at birth, and in the ability of the newly born infant to adapt to extrauterine life represent the greatest threat to infant survival and are intensively studied. Paramount in reducing the number of infants born prior to term is determining the cause of premature labor and how to retard early labor to enable optimal fetal development. Currently under investigation are intensive studies of placental physiology, biochemical "markers" of fetal maturation, and fetal monitoring. Electronic and biochemical monitoring of the fetus during labor and the process of birth has advanced significantly so that this technique is being utilized clinically.

An expanded research program aimed at solving the problem of the sudden infant death syndrome is underway and will continue. Several emphasis areas are identified for investigation: abnormal sleep patterns related to breathing and circulation and other functions essential to life; respiratory, heart, and circulatory responses to such stimuli as excess carbon dioxide in the blood or oxygen deficiency which may make certain babies likely to die of SIDS; the body's system for temperature regulation and its response to environmental conditions existing at the time of death from SIDS; the baby's developing immune system and how defects in development may predispose an infant to SIDS.

Studies in kittens demonstrated a relationship between the lack of spontaneous breathing and sleep patterns. Spontaneous apneic periods (cessation of breathing) occurred during both slow wave and rapid eye movement (REM) sleep. This work further demonstrated that sleep deprivation increased the frequency of apnea. Another investigator has found pathologic clues in the small lung arteries of SIDS babies that strongly suggest that chronic low oxygen saturation is associated with SIDS. Additional evidence of autonomic nervous immaturity and the controlling mechanisms of heart function in infancy have been documented in a SIDS victim during the past year. Futhermore, the interrelationship between apnea, heart rate, and the influence of state of sleep on the incidence of apnea in infants less than 5.5 pounds was firmly established last year. Using another scientific approach researchers continue to test the role of viral infections in SIDS. Sophisticated studies in viral localization are underway to test theories regarding respiratory insufficiency as a cause of death.

Mental Retardation

The mental retardation program is dedicated to research in the biological, medical, behavioral and social aspects of mental retardation within the context of child health and human development. This program embraces all factors that influence subnormal mental development. The objective of this program is to develop and support research to prevent mental retardation and, when this may not be possible, to effect its amelioration.

There are varied types and causes of mental retardation. The significance of mental retardation when considered in the aggregate is astounding. Approximately 6,000,000 American citizens are mentally retarded. More than 20,000,000 citizens are directly affected by mental retardation if one considers the immediate family members in addition to those who are suffering from the problem. Human suffering, however, is not the sole significance of mental retardation. Originating in early childhood and continuing through life, mental retardation is one of our nation's greatest long-term public health, social and economic problems. The economic loss to the United States caused by the problem is staggering. Estimates place the costs to assist the retarded in their intellectual and social development at over $3 billion annually. Social costs, defined as the increase in well-being that would occur if the retarded had the same level of vocational and social attainment, and required the same developmental expenditures as the general population, are placed at $5.5-6.0 billion every year.

Program Plans, 1975

Varying estimates have been made on the incidence of genetic disease concerning mental retardation. Although some forms of retardation such as Down's Syndrome (mongolism) are known to be genetic in origin, estimates vary due to the absence of accurate and comprehensive studies on the incidence of genetic defects as well as the difficulty in ascertaining whether a given defect is of genetic or environmental origin or the result of an interaction between the two. An estimate indicates that more than 2 percent of the population suffers from diseases or congenital defects which are inherited according to Mendelian laws. Another 5 percent have disorders in which both environment and heredity tend to be associated with the development of the disease. This area of neglect will be pursued in 1975.

An organized multidisciplinary approach to the problems of intrauterine diagnosis will facilitate rapid development in the area of characterizing genetic and metabolic errors, in order to identify those disorders that can be diagnosed before birth. The need exists to map human genes as a practical means of diagnosing disease. Program plans include follow-up on many of these promising areas of scientific opportunity as well as probing some of the most potentially productive scientific suggestions in this area, particularly: research dealing with gene localization and management of genetic disorders through organ transplantation; intergenic complimentation and the use of bacterial viruses which contain the enzyme missing in a specific disease; and continued use of tissue culture which will help verify genetic heterogeneity and other important genetic factors.

Research at the genetic and cellular levels is combined with research at the organism and behavioral levels because of the complex interrelationships that all factors play in either producing or preventing retardation. Mental retardation many times is congenital and in many instances is found in conjunction with other congenital defects. Studies dealing with the mechanism of action of various agents causing congenital defects will continue. The behavioral concomitants of physical malformations will be studied in relation to mental retardation as well as the developmental pattern of people who have received agents that could have caused physical defects but did not.

Infectious diseases pose a major problem because of the difficulty in linking the infection with the damaged central nervous system. In addition to developing and applying vaccines to prevent infectious processes, scientists will also attempt to gain a better understanding about the so-called slow and latent viruses. Specifically, the etiology of Reye's syndrome, a potentially preventable condition characterized by vomiting, rapid development of coma, and convulsions generally following an acute infection, will be studied. Work concerning H. influenzae type b must continue because it is the most common etiologic agent in childhood. Meningitis, a disease that can cause mental retardation and other health problems, is the most common disease produced by this organism. The development of an animal model is necessary to permit evaluation of: the route of infection of the central nervous system; protective mechanisms involved in the infectious process; effects of infection on cerebral metabolism; relationship between neurochemical events and neuropathological changes; and the nature, extent, and mechanism of cerebral dysfunction on surviving animals.

Although no direct causality has been demonstrated between malnutrition and human retarded intellectual development, highly suggestive evidence has been accumulated from numerous scientific investigations. Research will focus on the improvement of early diagnosis of malnutrition. Efforts will be made to provide information on how best to prevent it at any point in the life span; means will be sought by which the effects (including the suspected mental ones) of early malnutrition may be reversed; and, if the damage is reversible, the most efficient and effective means for achieving reversal will be determined. The mental retardation research in this field will effectively supplement and complement the low birth weight endeavors in the perinatal biology and infant mortality program and the nutritional efforts in the growth and development program.

Whatever the origin of mental retardation, it is always expressed via brain dysfunction. The ability to learn and to adapt resides in the brain; therefore, lack of these abilities must reflect dysfunction of the brain. Research in neurobiology at clinical levels is essential, especially to improve diagnosis and treatment of so-called minimal brain dysfunction. In the past, for example, attempts to use classical EEG and neuropathology methodologies were not very successful in expanding knowledge of mental retardation. However, new techniques such as computer averaging of EEG signals, measurements of auditorily or visually evoked potentials, liquid and gas chromatography, electron microscopy, and others place us on the threshold of a new era. Utilization of these techniques will make possible detailed examination of neurological, biochemical, and ultrastructural components of brain function and development in animals and humans heretofore beyond research capability. Fundamental approaches to the central nervous system disorders will now be undertaken with realistic success expectations.

Because of constraints imposed by the limitations of medical diagnostic procedures and development tests for infants, mental retardation is usually not detected early. A delay of almost four years for a diagnosis of retardation in those mildly afflicted and over one year for the profoundly retarded points to the need for advancing diagnostic capabilities. Early diagnosis is critical because studies have provided evidence supporting the effectiveness of early intervention for improving the development of retarded children. Research, therefore, will continue in the areas of diagnosis and intervention so that appropriate early intervention will eventually be available for comprehensive clinical utilization.

Two specific diagnostic and intervention research areas will be enriched. The first area concerns studies in prenatal diagnosis of conditions associated with biochemical, genetic, and physical disorders and the development of therapeutic programs which can be applied prenatally to correct those conditions. The second is a research effort aimed at providing diagnostic means for the early identification of infants at high risk for faulty development, with parallel investigations of the effects of intervention methodologies on their development.

In addition to intervention, treatment and amelioration programs must be continued. Excepting some inborn errors of metabolism such as PKU (phenylketonuria) and galactosemia, there are few remedies available today by which organic defects can be corrected. The search for treatments will be continued. For individuals who cannot be treated at present, the prevention of secondary handicaps or efforts to minimize the debilitating effects of the primary handicap through education, rehabilitation or training are major research goals. In the final analysis, the amelioration or treatment of mental retardation involves helping the handicapped to a higher level of functioning and adaptation to the environment. The institutional environments for the severely retarded commonly deprive the patients of opportunities for social expression and meaningful human interactions, and not surprisingly, many individuals deteriorate even further in such a stultifying environment. Research leads that show positive results when such environments are altered will be followed-up.

Among the various handicaps shared by the mentally retarded and others with developmental disabilities, communication disorders are probably the most common. Ten to 15% of the retarded have communicatively significant hearing impairments; over 70% have some form of speech disorder, with many of the more severely retarded having no functional speech; and almost all retarded individuals have some degree of language deficiency. The mental retardation program and the growth and development program are encouraging a wide range of research activities dealing with communication disorders. Recent emphasis in mental retardation research regarding hearing focuses on the relationship between hearing impairment and language deficiency. In 1975, more research emphasis will be given to the question of how children develop articulatory or phonological systems since articulation errors are the major speech problem in both retarded and non-retarded children. Research into the language problems of the mentally retarded will be continued.

Research will also be continued concerning broader environmental factors. An estimated 75% of the retarded population are mildly retarded and scientists to date have not been able to clearly demonstrate central nervous system disorders in these individuals. Recent results indicate that there is the distinct possibility that among the many variables associated with poverty and deprived living conditions - poor diet, inadequate health care, lack of organized mental stimulation, broken homes, limited educational and social opportunities - none stand alone as causative factors in mental retardation. As a syndrome, however, or in various interactive combinations, the additive effects may prove highly detrimental to development and behavior.

Many of the accomplishments described later and many of the program plans for 1974 and 1975 involve the Mental Retardation Research Centers. The Centers program is a unique resource for multidisciplinary and collaborative research between biomedical and behavioral scientists to better understand the complex causes, pathogenesis and modes of prevention, treatment, and amelioration of mental retardation. An important adjunct to research is the testing of new ideas in practice, the clinical application of preventive and treatment modalities and the training of manpower to staff emerging service programs. In 1974 and 1975 there will be approximately 600 investigators and 1,200 support personnel working in the twelve Mental Retardation Research Centers:

University of Chicago
Chicago, Illinois

Children's Hospital
Cincinnati, Ohio

George Peabody College for Teachers
Nashville, Tennessee

University of Colorado Medical Center
Denver, Colorado

University of Washington
Seattle, Washington

University of California at Los Angeles
Los Angeles, California

Albert Einstein College of Medicine
Yeshiva University, New York, New York

University of Kansas
Lawrence, Kansas

Walter E. Fernald State School
Waltham, Massachusetts

Children's Hospital Medical Center
Boston, Massachusetts

University of North Carolina
Chapel Hill, North Carolina

University of Wisconsin
Madison, Wisconsin

In 1975, the major significance of the Center effort will be to tie together all of the pertinent research leads and if applicable follow them through to practice. The ultimate goal is to combine the development of objective clinical, laboratory, psychological, and environmental criteria for screening, early detection, differential diagnosis, and eventual treatment and amelioration of mental retardation.

Program Plans, 1974

Recent years have witnessed a significant growth of scientific technology which has resulted in a better understanding of the chemical structure of hereditary material, better knowledge of the exact biochemical mechanisms of many hereditary disorders, application of computer technology for genetic analysis, and increased use of tissue culture to understand several types of genetic disorders. Geneticists can now accurately identify each chromosome in the human complement by the application of different banding techniques. The structure of each chromosome can be better characterized by applying different staining techniques. These fundamental research results in genetics, coupled with similar results in other fields related to mental retardation, have provided the bases for accomplishment and further scientific probing.

Recent research has resulted in a better understanding of a number of genetic conditions and inborn errors of metabolism that can be diagnosed. Investigations are currently underway to perfect animal models which will permit intensive investigations in PKU (phenylketonuria). To date, biochemical data obtained confirm previous reports that the behavioral and biochemical aspects of experimentally induced PKU are similar to those of the human retarding disease. Thus, the model may be used in the future to correlate nutritional, metabolic, and functional components of certain aspects of behavior in both normal and PKU diseased situations so that eventually behavior may indicate specific functional, inborn metabolic or genetic difficulties in humans. Investigators are presently completing field tests to evaluate two new low-cost, simple methods (that can be combined easily with current PKU screening programs) to detect galactosemia, a metabolic error that does not permit an infant to consume milk and milk products because of probable liver or brain damage.

Important progress is being made in the area of gene localization by using tissue culture methods with cell hybrids. By using selective media, preferential loss of human chromosomes can be achieved which then enables investigators to determine in which chromosome a particular gene is located. By using this method, particularly with morphologically distinct chromosomes, one can also delineate in which segment of a chromosome a gene or genes are located.

Early diagnosis and intervention research is progressing. Amniocentesis (obtaining fluid from the uterus) has become an invaluable tool for prenatal diagnosis of mental retardation. This diagnostic technique can seldom be performed before 16 weeks of pregnancy, then it takes 3-4 weeks to grow cells in tissue culture sufficient for chemical analysis. This waiting period increases the anxiety of the patient. Promising techniques are being developed to accelerate the growth of these cells by creating a more favorable condition in the culture medium for cell growth.

Many brain damaged children are distractible, hyperkinetic (over active), emotionally unstable and unable to learn. Amphetamine, normally a stimulant, has a paradoxically calming effect on these children, but the mechanism is unknown and difficult to study in children. Investigators at a Mental Retardation Research Center have produced an animal model, deficient in serotonin (a blood platelet constituent) in which this drug has a similar effect. It is postulated that serotonin is responsible for inhibition in the normal child and that the hyperkinetic child is deficient in this chemical. It is hoped that dietary supplementation of this chemical may be therapeutically useful, thus avoiding the disadvantages of amphetamine.

Through the Mental Retardation Research Centers program, scientists are continuing to seek solutions to many of the problems previously described. One research staff, for example, is conducting detailed clinical and genealogical observations of retarded persons and their families from the metabolic research approach directed toward diagnosis and treatment. Program plans call for the development and applications of techniques for the study of storage substances in tissues and body fluids and for the study of basic biochemical deficits in tissue culture. Center scientists have contributed new and significant knowledge on the relationship among nutrition and brain development, cell size and cell number. The continuation of nutritional and other environmental research is planned in 1974 and 1975. Three Mental Retardation Research Centers are undertaking major efforts in the epidemiology of mental retardation - its incidence, prevalence, mortality, morbidity, geographic and demographic factors, and the conditions with which it is associated. The expectation is that significant clues to the search for causes and loci for intervention will be found.

These Centers, located throughout the country, are uniquely capable of carrying out research in the complex problems of mental retardation because they are conducive to multidisciplinary endeavors. The knowledge gained through the clinical studies conducted at these centers makes possible immediate contributions to the communities in which they are located.

Growth and Development

Research attention in the growth and development program focuses on the child from infancy to maturity. Included within the program's scope are the physiological as well as the behavioral aspects of child health and development, with particular emphasis given to the interplay between these diverse processes. It investigates those time-related factors within the individual and his physical and social environment which direct his development and prepare him for adulthood. Ultimately the goal of the research supported by this program is to help the child become an independent, healthy, and productive adult.

The 1970 census showed that there were 41 million children in the United States 10 years of age and younger; another 32 million youths and adolescents 11-18 years of age were identified. Of these children, more than 7 million are handicapped. Most of them have communicative disorders and learning disabilities. However, the list of associated problems, too many to fully enumerate, includes: retarded growth, anemia, obesity, behavioral problems such as drug abuse, and other problems that may permanently prevent assumption of a fully functional adult role. The problems encountered here relate to the interdependence of the life span from perinatal biology to the process of aging. The study of normal growth and development will help us understand many of these developmental problems and thus be able to prevent or ameliorate them.

Program Plans, 1975

Continued emphasis regarding susceptibility to disease will be directed to the control mechanisms acting throughout the life span which govern the development of full immunologic competence. Emphasis will also be turned in the direction of the effects of malnutrition on the immune system since past results prove that increased morbidity and mortality are known to exist in undernourished populations. Further studies of the secretory immunologic system, involving regional immunity mediated by locally formed antibody found in the external secretions of humans, will be initiated. In general, those areas of immunology that show immediate avenues for scientific opportunity will be explored.

Nutrition and infectious disease interactions, and augmentation of the area of developmental immunology with a holistic philosophy concerning body defenses against body infection and disease in the developing infant and child, is another area of research which will receive continued emphasis.

Growth failure research will continue to probe the determinants of physiologic development and growth at both the cellular and tissue levels. Research plans include studies directed toward the identification of chromosomes which carry mutated genes that result in hereditary growth failure.

Research aimed at identifying the active site of the growth hormone molecule will continue. Continued research to augment the yield and lower the cost of production of the synthetic growth hormone molecule will be undertaken. Ultimately these efforts will merge into one goal; namely, the high yield synthetic production of the active fragment of the human growth molecule.

Nutrition is an important area of biomedical research that requires continued attention. However, as scientific opportunities arise, the Institute plans to alter its nutrition emphasis into areas that should be as equally productive as those already under investigation. Limited data, for example, are available concerning nutrient requirements of adolescents. There is a need for a better understanding of the relationship between nutrition and intellectual development, with special attention to social-environmental factors including the potential impact of malnutrition on the ability and motivation of the child to participate in learning experiences. Little is known of the effects on physical and intellectual development of the moderate or subclinical undernutrition more frequently encountered in this country. The relationship of behavioral developments to social variables which surround poverty and malnutrition are not understood. Special attention will be given to unravelling these variables and to determining whether rehabilitation or preventive programs will require medical, nutritional or educational interventions alone or in combination. Although there will be a shift in emphasis, the basic problem of elucidating the nutritional correlates of normal development and the developmental consequences of nutritional deprivations or disorders will serve as a nutrition research framework.

The problems in hearing, speech and learning are receiving a multi-faceted research attack from many NIH programs, including the Institute's mental retardation program and the growth and development program. Although the programs necessarily interrelate, the growth and development program concentrates on the normal process of learning and behavior. To understand how children learn to communicate and develop these skills which are required to become contributing members of society, more complete knowledge must be acquired concerning the development of the speech- and language-producing mechanisms, the phylogeny and ontogeny of intellectual development, and how the communicative and intellectual processes merge in the human. While continuing to look at the young child during the formative years, the program plans to stimulate studies of the dramatic changes in communicative patterns which take place during adolescence and the effects of these rapid changes on the growth and development of youth.

Of major scientific importance is the area of adolescence. Scientists have realized that there is a critical need for research leading to a better understanding of the biological and behavioral problems unique to this developmental period, research that may lead to a plan for modifying our social, psychological, and medical treatment of America's youth. Presently, data regarding the nutritional requirements of adolescents are very limited, and resolution of identified problems will depend a great deal on a better characterization of these nutrient requirements, maturational status and physical growth during adolescent development. Further studies will be undertaken regarding the etiology, prevention, or amelioration of obesity especially in adolescence, because of the medical, social and economic implications of this disease state. Behavioral development, including cognitive and social processes and the interaction between adolescents and social groups is an area of particular need and will be emphasized in 1975. Studies will be undertaken to elucidate the effects of early experience upon the developing brain and the subsequent behavior of children. The major focus of this program will be to clarify the neurological consequences of a) maternal-social deprivation; b) isolation of the young; and c) various forms of institutionalization of children.

Program Plans, 1974

Susceptibility to disease has, of course, been of interest to both the lay and scientific publics. Special attention is being given to the development of immunologic competence as a function of age, with emphasis on the fetal, newborn and infancy periods, but with a continuing interest in older age groups as well. Recent research progress shows that it is increasingly apparent that the impact of immunologic mechanisms used to combat infections and foreign substances (environmental pollutants, drugs, etc.) on immune development early in life may also program response to disease in adulthood and aging. Research in immunology has demonstrated that the normal major immunological defense mechanisms are acquired as early as mid-gestation in most mammals. This finding is of special significance because it was previously assumed that the unborn or newborn infant was immunologically inert. As a result of immunologic research, a few diseases have been found to be treatable - in fact the effort has proven to be lifesaving in some cases.

Growth failure research has directed its attention toward the determinants of physiologic development and growth at both the cellular and the tissue levels. Although progress has been made regarding some types of growth failure (hypopituitary dwarfism and delay of puberty, for example), many appropriate treatments are extremely expensive and not fully understood. For the more than 2 million children in the United States that are deviant in stature, major research thrusts are aimed at increasing the supply of growth hormones for children and identifying parameters that may reliably predict mature stature of growing children.

The growth and development program is continuing its nutrition research program in 1974. This program is closely coordinated with the nutritional research being pursued in the mental retardation and perinatal biology and infant mortality programs so that an optimal utilization of resources will produce accomplishments for all child health endeavors. Major results regarding the impact of malnutrition in pregnancy in terms of the development of the progeny have been reported. The intimate interaction of nutritional, behavioral and social variables has been established and rapid progress is now being made toward a specific definition and quantification of each. Studies have also provided an improved description of physical growth and body composition in relation to the age, sex, and nutrient intake of normal infants receiving either breast milk or cow's milk. The amino acid, protein and energy requirements for normal infant growth also have recently been defined with greater precision than was available heretofore. The hormonal interrelationships of adipose (fat) tissue cellularity and the mechanisms by which obesity in young children predisposes the individual to adult obesity have also been recently reported.

In the area of learning and human communication, recent studies have shown that within the first week after birth infants are able to discriminate between such speech sounds as /bah/ and /gah/. This is important in itself, but the learning implications are astounding because these infants perceive the sounds in an all-or-none categorical manner, as do adults, hence, presumably, in a linguistic mode as opposed to a purely acoustic one. Findings such as this will be followed-up as will the recent research accomplishment involving college students. Investigations have shown that entering college freshmen, based on factor analyzed life histories, fall into a limited number of definable subgroups which are predictive of a wide range of behavior and performances four years later. The implications of this research for a broad range of intervention strategies is enormous.

Aging

Authorizing Legislation: Public Health Service Act, Title IV, Part E

	1974 Base *		1975 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits...........	---	---	---	---	---	---
Other expenses...........	---	$10,970,000	---	$9,078,000	---	-$1,892,000
Total...........	---	10,970,000	---	9,078,000	---	-1,892,000
Budget Mechanism:						
Research Grants:						
Regular..............	---	8,659,000	---	6,366,000	---	-2,293,000
Special..............	---	139,000	---	95,000	---	-44,000
Subtotal...........	---	8,798,000	---	6,461,000	---	-2,337,000
Fellowships............	---	371,000	---	661,000	---	+290,000
Training Grants.........	---	1,136,000	---	1,156,000	---	+20,000
Research and Development Contracts........	---	665,000	---	800,000	---	+135,000
Total...........	---	10,970,000	---	9,078,000	---	-1,892,000

Introduction:

The Aging program supports research on the multitude of biological changes that occur with aging and are major determinants of disease processes, studies of cognitive and emotional alterations that occur with increasing age, and investigations of societal aspects of aging. Currently, the areas of research emphasis are the menopause, aging of the immunologic system, cellular aging, and the impact of improved health and increased longevity on society and on individuals.

The aging extramural research program is accomplished through the award of research grants, fellowships, training grants, and research contracts. Within the Institute, aging research is conducted at the Gerontology Research Center in Baltimore, a major intramural effort providing facilities and resources to both NICHD and non-federal scientists who wish to pursue research in this field. The funds and description of programs for the intramural research effort in aging are contained within the activity Intramural, Laboratory and Clinical Research. The funds to support the staff necessary to provide the scientific and administrative management of the aging program are contained within the activity Research Management and Program Services.

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* Excludes 1973 appropriation restorations.

Program Plans, 1975

In a number of ways aging in women differs from aging in men. For example, as age increases, bone fragility is much more pronounced in women. A deepened understanding of the aging process in women should benefit both sexes, and this process will continue to be a major focus of the aging research program. Concentration will be on the causes, results, and treatment of menopause. Studies of the menopause will be continued in 1975, and the scope of the program will be modified to include investigations of changes with age in androgenic and related hormones in man, and additional retrospective and prospective investigations of hormonal treatment of the menopause.

Utilizing many of the known risk factors, the Institute plans to support the development and refinement of a system for individualized preventive medicine. Promising leads will be followed concerning the systematic development of risk factors (overweight, high blood pressure, smoking habits, etc.) in preventive medicine for the elderly as well as the general adult population. Advancements regarding risk factors in various longitudinal studies will pave the way toward developing preventive medical techniques to make the old age years dignified, independent, and productive.

The science of nutrition, having identified dietary factors required for health, will be turning increasingly to search for diets and supplements which affect the aging process itself or which are designed to modify age-related diseases. Mounting public concern about the impact of environmental and nutritional factors on life and health mandates further emphasis in 1975 on aging research in these areas.

In the area of immunology and aging, studies of the effect of several variables on aging of the immune system will proceed. Funding for immunological studies will be used to explore further the leads already established in the program. In addition, efforts will be continued to develop sources of aged experimental animals for use in these studies.

Related to the immunology studies is research on aging at the cellular and molecular levels. Understanding the fundamental processes of aging at the cell level of an organism will eventually open the doors to understanding the aging process of the organism as a whole. In 1975, the aging program will continue to investigate these cellular processes, including synthesis of molecules which transmit information to new cells, and the cell's ability to reproduce itself. In addition, studies will be concerned with the mechanisms controlling the reproductive potential of human cells and methods for modifying this potential.

Continuing efforts involving the societal aspects of aging will be undertaken in 1975. Ongoing studies of the age-structure of the human population and the impact of changing mortality rates will be refined in 1975, with the objective of linking these characteristics with environmental factors which influence the age-structure. The implications of these findings will then be investigated, toward the development of scientific bases for planning ways in which the individual can best be prepared for retirement years, or for developing societal institutions to serve the elderly most beneficially.

Program Plans, 1974

Research on aging in women is in its formative stages. The Institute has recently concentrated on the study of the menopause. The great reduction in the ovarian excretion of estrogen following the menopause causes changes in the genital tissues, hot flashes, and sweats. It has been known for several decades that those symptoms can be eliminated by the administration of estrogenic hormones. However, a great deal remains to be learned about who needs this treatment, what the best preparations are, what the dose schedule should be, and what the undesirable results of such therapy may be. Part of the individual variation in menopausal symptoms is related to the production of estrogenic hormones in tissues other than the ovaries. The Institute has been supporting research on these topics for several years. During 1974 Institute-supported research has shown that the production of estrogens by such tissues is considerably greater in postmenopausal women than in those in the reproductive years of life. Variation in this extraovarian production of estrogen may explain the greater need of some women for replacement therapy than others. The Institute is also supporting an ongoing study of undesirable side-effects of replacement therapy in the menopause.

It has recently been discovered that there is a striking diminution in immunological competence with increasing age. The decline is so great that the elderly retain only one-tenth of the peak immune capacity shown during adolescence. Experimental animal studies are now underway to determine whether the immunologic deterioration that occurs with age involves changes in the function of individual cells, changes in the number of specific cells present, or changes in the microenvironment in which they operate. The marked deterioration in immune function that occurs with age is important because it predisposes the middle-aged and elderly to infections, cancer, and autoimmune disease. The development of means of augmenting immune competence in the later years of life would represent a major advance in improving the health of older people.

Recent studies have shown that caloric restriction, known to prolong the lifespan of rodents, significantly reduces the decline in immunologic decay that occurs in them as they age. This discovery may provide a lead to the prolongation of immunologic competence in man. Studies of the effect of several variables on aging of the immune system will be expanded in coming years. Efforts to determine the exact locus of the change in immune function will be made.

Although complex systems such as the endocrine and immune systems may be modified to control some aging manifestations, more vigorous intervention might be possible if the cellular processes damaging these systems were understood. The progress of modern biology has provided concepts and methodology to investigate those processes. Through tissue culture and transplantation studies, scientists have learned that normal mammalian cells cannot reproduce themselves indefinitely. This knowledge has caused a profound change in theories of aging by emphasizing that an understanding of organismic aging has to be based on cell biology. In the past year the cell whose limited ability to reproduce itself has been most intensively studied is the human cell that builds the supportive structures of the body.

Recent work has shown a correlation between the age of cells in tissue culture and their ability to synthesize the molecules that transmit information to the new cells obtained when old cells divide. An adrenal hormone has been shown to prolong the lifespan of cultured populations of cells. The mechanisms involved in this are under investigation.

The future age-structure of our population will depend on the transformations wrought in the current age-structure by future natality, migration, and mortality rates. Because the age-structure has great implications for society (health care, transportation needs, etc.) a mathematical model, probably computerized, is needed into which can be fed estimates of those rates for future years and data on the present population structure. The Institute is supporting studies of the currently existing models, and is investigating possible developments to increase their suitability to the task at hand.

Changes in mortality due to control of diseases and moderation of aging processes will influence the age-structure of the human population and thus affect in many ways society as a whole and the individuals who compose it. The Institute is currently supporting studies that may enable society to evaluate the possible future impact of changing mortality rates.

The studies to date have been based on extreme assumptions but are useful in outlining possible limits to the shape of the future. With no reduction in mortality rates a population over 65 years of age of somewhat less than 30 million people may be expected in the year 2,000. With the gradual elimination of vascular disease such a population of almost 40 million seems likely. The elimination of any other category of disease would increase the population much less. The aging program is continuing to study the implications of this increased population, to develop plans by which society might adjust to the situation, and even prepare for it.

Intramural, Laboratory and Clinical Research

Authorizing Legislation: Public Health Service Act, Title IV, Part E	1974 Base		1975 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits............	338	$6,808,000	348	$7,215,000	+10	+$407,000
Other expenses...........	---	7,417,000	---	7,512,000	---	+95,000
Total...........	338	14,225,000	348	14,727,000	+10	+502,000
Budget Mechanism:						
Laboratory and Clinical Research..............	323	13,519,000	333	14,012,000	+10	+493,000
Biometry, Epidemiology and Field Studies.....	15	706,000	15	715,000	---	+9,000
Total............	338	14,225,000	348	14,727,000	+10	+502,000

Introduction:

The Intramural, Laboratory and Clinical Research program comprises the Institute's intramural effort, including biometry and epidemiology, in the three major program areas of population and reproduction, child health and aging.

Eleven laboratories and branches conduct the intramural research operations in the program areas of the Institute. These include the Social and Behavioral Sciences Branch, Reproduction Research Branch, Laboratory of Biomedical Sciences, Developmental Immunology Branch, Behavioral Biology Branch, Pregnancy Research Branch, Laboratory of Molecular Genetics, and Gerontology Research Center (Baltimore) - composed of the Laboratory of Molecular Aging, Laboratory of Behavioral Sciences, Laboratory of Cellular and Comparative Physiology, and Clinical Physiology Branch.

The Office of Epidemiology and Biometry supports the Institute's staff in planning and conducting studies dealing with the incidence, prevalence and other characteristics of the diseases and abnormal conditions occurring in pregnant women, infants, children and among the aged. This activity also supports research into the theory and methodology of statistics, the collection and analysis of data sets providing current trends in vital statistics, and the development of more effective and reliable means for measuring health problems relating to the research objectives of this Institute.

Program Plans, 1975

Laboratory and Clinical Research - The focus of the intramural research program in population is the development of scientific data and theory basic to reproductive biology, from the chemistry of hormones to physiologic and clinical studies in man, which may be applied to the development of safer and more efficient contraceptive agents. In 1975, all the major areas of effort in 1974 will be continued, with particular emphasis on the biology of spermatogenesis, ovulation, fertilization, implantation, and the process of male gamete formation, with the eventual objective of interrupting the reproductive cycle for contraception. Increased emphasis will be placed on the study of male infertility, its causes and treatments. The number of visits to the Institute's infertility clinic is expected to increase markedly in 1975, as research is intensified to identify the reasons for infertility and discover methods to correct it.

An assay developed in 1974, which measures and discriminates between two hormones which indicate pregnancy, will continue to be tested in 1975, and modified to make its principle applicable as a procedure which can be performed in the physician's office. This assay can determine pregnancy by the 8th day after conception, 3-4 weeks earlier than was previously possible. Other applications of this test include allowing diagnosis of difficulties such as tubal pregnancies, and the detection of tumors which produce minute amounts of these hormones.

In 1975 the major focus of the Institute's intramural _child health_ program will be the expansion of a research program in perinatal medicine. Researchers in this effort will intensively study the physiologic changes of pregnancy, delivery and adaptation of the newborn, with the goal of increasing understanding of this complex process so that maternal and infant care may be improved and morbidity and mortality may be further reduced.

Clinical trials will continue to assess the effectiveness of a vaccine developed by Institute scientists to provide infants with immunity to _Hemophilus influenzae_ meningitis, the leading cause of acquired mental retardation.

Other programs are continuing on the high-risk obstetrical patient and the physiology of the neonatal period. To define the processes of fetal and early childhood development, programs are being conducted in developmental biochemistry, information transfer, neurophysiology, child psychology and environmental influences on childhood maturation. The effectiveness of preschool stimulation in various environments continues to be evaluated to develop the most effective means of preparing children from deprived environments for adaptation to school situations.

Current studies are investigating the interaction between infant characteristics and maternal behavior, and their relation to acquisition of information by the child. Rather than viewing the infant simply as a passive recipient of stimulation, these studies assume that the infant actively interacts with his environment, eliciting behavior from his mother and others, and through his individual sensitivities selectively filters and moderates environmental events. These studies will increase understanding of early family interaction, and its effect on child development, as well as help scientists suggest more ideal environments for young infants so that information acquisition in the early school years will be facilitated and strengthened by an existing sound base. Research in this area will be continued in 1975, and expanded to emphasize evaluation of father-infant interactions as well.

Scientists at the Gerontology Research Center in Baltimore conduct the Institute's intramural research on aging. A major activity is the continuation of the ongoing longitudinal study. This is an effort to obtain a detailed understanding of the aging process by making periodic biochemical, physiological, and psychological observations of the same male as he ages. Analysis in 1975 of much of the data obtained in this study will begin to identify changes which characterize aging in contrast to those resulting from disease.

Research on the age-related change of the immunologic function in humans will be intensified in 1975. New techniques will be used to investigate one theory into the cause of aging, the hypothesis that the body's cells become slightly altered with age, and then become antigenic themselves, stimulating production of an antibody which then destroys both the new abnormal cells, and the normal ones.

Epidemiology and Biometry - In 1975, the epidemiology and biometry program will continue its research efforts directed toward obtaining a better understanding of the epidemiology of prematurity, prenatal, neonatal and infant mortality and other high risk factors for the abnormal development of children. The particular emphasis of these activities in 1975 will be the sudden infant death syndrome, the leading killer of infants between one month and one year of age.

In addition, data collected in 1974 on the risks of the diagnostic procedure amniocentesis will be analyzed and followed-up in 1975. A study on the effects of phototherapy in infants with bilirubinemia will continue through 1976. Staff will also continue to provide statistical and epidemiologic support to all the Institute's programs.

Program Plans, 1974

Laboratory and Clinical Research - Programs in reproductive biology stand at the center of intramural population research. From scientists in these laboratories have come virtually all the new precise techniques for hormone measurement which have led to numerous recent clinical advances in endocrinology. These efforts are the source of practical solutions to problems of population growth, since new knowledge of reproductive physiology is the essential ingredient for practical applied programs.

In the past year sensitive assays have been developed by scientists in this program which measure and discriminate between human chorionic gonadotropin (HCG) and luteinizing hormone (HLH), whose relative levels indicate pregnancy. These assays are so sensitive that scientists can now detect HCG as early as the 8th day after conception. Thus, pregnancy is detectable unambiguously 3-4 weeks earlier than previously possible. This test is being adopted in research centers around the world. The test has a number of potential clinical applications. For example, because it indicates the existence of a pregnancy so soon, it assists physicians in diagnosing an ectopic (tubal) pregnancy in a woman with abdominal pain. In addition, the assay has discerned ectopic production of an HCG-like hormone by a series of human tumors not previously known to have the capacity for HCG synthesis. The assay has proven uniquely useful for detection of these tumors and for following the response to treatment by women with uterine tumors.

The Infertility Clinic, established in 1971, provides an environment for evaluating problems of infertility. During 1974, both male and female patients will make an estimated 3,800 clinic visits. One of the first scientific results from this clinical research has been a description for the first time of the pathogenesis of the short luteal phase as a cause of female infertility, and its successful treatment. This program will be continued in 1975 and additional patients will be accepted.

The child health segment of the intramural program is concerned with improving the quality of life of the nation's children through biomedical research. Programs encompass research on pregnancy, the infant, and the developing child. Investigators employ a broad range of disciplines, including sociological, psychological, biological, and behavioral, in their research on the child and his environment. Areas of particular interest include developmental immunology and pharmacology, and the sociology of the family, as they relate to mental retardation, infant mortality, and the growth and development of the child.

In the area of developmental immunology, both basic and clinical research will continue into the development of immunity during the intrauterine and neonatal periods, and infancy. The leading cause of acquired mental retardation, Hemophilus influenzae meningitis, may be fully preventable if findings of the Institute's scientists are borne out in recently initiated human trials. Research by Institute scientists with this organism has resulted in development of a vaccine, which employs the capsular polysaccharide of the organism to stimulate production of antibody and induce immunity. A clinical trial of this vaccine began in 1974 in Mecklenberg County, North Carolina, under the Institute's auspices. Meanwhile, extensive animal testing is continuing to assess safety and efficacy of the procedure of feeding newborns harmless bacteria which stimulate immunity to H. influenzae, as an even better way to prevent the disease.

Investigators in the intramural program have been systematically studying drugs and environmental contaminants which can cross the placenta to influence the fetus, and the mechanism by which these agents act. These scientists have recently discovered that fetal cells in tissue culture respond, in terms of capability of enzyme induction, in the same way as the intact animal, and reflect genetic variations in this trait. Thus, by means of studies in cell culture, the toxic effect in the intact animal of the substance being tested could be predicted. This finding may make it possible to assess the potential teratogenicity (the tendency to produce malformations) of various drugs or other foreign compounds in genetically different individuals by tissue culture studies.

A study completed in 1974 by other intramural scientists has important implications for the ever increasing number of working mothers whose children have substitute caretakers for part of the day. The mothers and caretakers were compared on measures of infant stimulation and interaction important to infant development. Mothers provided more stimulation than surrogates on all measures tested. Nonetheless, the difference did not have a measurable effect on infant functioning when the children were tested at 18 months.

The longitudinal study of the physiological, biochemical, and psychological aspects of aging is continuing at the Gerontology Research Center in Baltimore.

This year techniques have been developed to define the needed frequency of data acquisition and number of subjects needed in order to define the rates of aging changes in selected functions with specific accuracy. These techniques have applicability for longitudinal studies in general. Additionally, the influence of lifetime nutritional experience on the declining years of life is being investigated both in the longitudinal study and in animal models. Data acquired indicate that dietary changes can modify longevity both adversely and favorably in animals, while in humans there is clear evidence of an age dependent change in micronutrient requirements. These studies must be continued at least to the stage where all of the factors that are dependent on age are identified.

Scientists in the Section on Immunology established at the GRC in 1974 are studying the mechanism of age-related changes in immunologic function in humans and animals. New techniques for immunological assays and investigations of the control mechanisms for antibody formation have made it possible to initiate new research efforts to identify changes in the immune system with aging. Decreases in immunologic competence have been found to occur with aging, and may be very important in the diminished resistance of the elderly to infection, and possibly contribute to the age dependent incidence of cancer. These scientists have observed that there is an increase with age in a class of lymphocytes that suppress the response of immunocompetent cells. This increase may be responsible for the depressed proliferative capacity of lymphocytes from older animals. Investigations to follow this lead are continuing.

Scientists at the GRC have recently extended their studies of the possibility of introducing substances, such as hormones, enzymes, and genetic material, into cells without injuring them, by attaching the substances to synthetic polymers. Further research has used these biological probes to introduce new materials into cells to assess their effect in repairing or counteracting the effects of aging. In addition, these synthetic polymers have been found to induce formation of interferon, a substance protecting the body against virus infections. Age appears to limit ability to make interferon, thus playing a part in increasing susceptibility to infection with aging. It is possible that these synthetic polymers may be used to artificially stimulate interferon production to help compensate for its decline with aging.

Epidemiology and Biometry - In 1974, a major activity of the Epidemiology Branch relates to various aspects of pregnancy, outcome of pregnancy and events occurring during the first year of life. Special attention has been given to a study whose purpose is to compare two prenatal nutritional regimens in a defined geographic area. The validity of the data collected has already been checked and analysis is near completion. Other studies in 1974 pertain to completing analyses of the interrelationships among the important variables of birth weight, gestational age and infant mortality. Another major effort begun during the year is directed toward an increased understanding of the role of certain physiologic processes such as sleep in the etiology of the sudden infant death syndrome. Sources of data for these studies consist of records obtained from state and local governments, in addition to special studies initiated and monitored by staff in the Epidemiology Branch.

The other area supported by this activity is the Biometry Branch. This program, in addition to conducting research in statistics and applied mathematics, also provides consultative services to intramural scientists and to extramural program staff on the design and analysis of laboratory and clinical experiments, community health surveys and clinical trials. In addition, this program serves as a data center for collaborative study on the risks associated with amniocentesis, a diagnostic prodecure used in early pregnancy. Data entry of cases into the study has terminated in 1974. The analysis of data and one-year follow-up are now proceeding and will continue into 1975. Another collaborative study on the use of phototherapy in infants with excess levels of bilirubin will start in mid-1974 and continue into 1976.

Research Management and Program Services

Authorizing Legislation: Public Health Service Act, Title IV, Part E

	1974 Base		1975 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits............	181	$4,077,000	181	$4,263,000	181	+$186,000
Other expenses............	---	4,248,000	---	4,269,000	---	+21,000
Total............	181	8,325,000	181	8,532,000	---	+207,000

This activity provides for the overall administration, direction, and coordination of the Institute's programs. It encompasses 1) the Director and his immediate staff concerned with administrative management, program planning and evaluation, and research information, 2) the scientific and administrative staff responsible for grant and contract programming, review and administration, and 3) the scientific staff associated with the Center for Population Research.

Program Direction - This activity provides assistance and counsel to the Director in the fields of management, financial planning, program and statistical evaluation, and analysis in the furtherance of the Institute's programs. During 1975, this activity will continue to provide the necessary professional leadership and technical guidance.

Extramural - This activity provides the necessary professional and technical guidance for the processing and scientific monitoring of the Institute's grant and contract programs relating to child health and aging. During 1974, approximately 858 grants, totalling $58,233,000, will be awarded. In addition, $4,729,000 in research contracts will be awarded.

In 1975, this activity will continue to provide the required technical guidance in the furtherance of the Institute's grant and contract programs. During this period approximately 957 grants will be awarded totalling $56,306,000. In addition, $5,050,000 in research contracts will be awarded.

Center for Population Research - This activity provides the necessary direction, review and scientific monitoring of the grant and research contract programs in the broad spectrum of population research encompassing biomedical and social sciences. During 1974, approximately 407 grants totalling $25,469,000 will be awarded. In addition, $13,969,000 in research contracts will be awarded. In 1975, the Center for Population Research will continue to provide the scientific and administrative support for the grant and contract programs of population research. During this period approximately 496 grants totalling $25,114,000 will be awarded. In addition $15,168,000 in research contracts will be awarded.

Program Services - This activity provides the necessary administrative management, negotiation, processing, and analysis of all of the Institute's grants and contracts. During 1974, 1,265 grants will be awarded totalling $83,702,000. In addition, research contracts totalling $18,698,000 will be negotiated and awarded. It is estimated that 20 research conferences will be held relating to the Institute's programs. In 1975, Program Services will continue to provide the necessary support for the processing and awarding of research grants and contracts. In 1975, approximately 1,453 grants totalling $81,420,000 will be awarded. In addition, research contracts totalling $20,218,000 will be negotiated and awarded. The Institute plans include the continued support of the research conference program in 1975.

NATIONAL INSTITUTES OF HEALTH

National Institute of Child Health and Human Development

Program Purpose and Accomplishments

Activity: Population (Public Health Service Act, Title IV, Part E)

		1975		
1974			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
---	$39,438,000	Indefinite	---	$40,282,000

Purpose: Population research encompasses four large and complex undertakings: contraceptive development, contraceptive evaluation, social and behavioral sciences, and fundamental population research.

Explanation: The research program encompasses the biological, medical, demographic, and behavioral aspects of population dynamics.

Accomplishments in 1974: The contraceptive development program for synthesis and testing of antifertility agents is currently in progress. In addition, clinical studies on the safety and efficacy of synthetic and natural estrogens as postcoital contraceptives have just been initiated. The contraceptive device effort has centered on improvement in sterilization techniques for males and females. The Institute's research on male sterilization techniques has produced several intra-vas devices which are designed to be reversible. Research in the social sciences has resulted in important findings regarding psychological, social, political, demographic, and economic issues related to population dynamics. Fundamental research has produced intriguing and important leads in such areas of research as the mechanism of fertilization and conception, prostaglandins, and the action of progesterone and other sex steroids.

Objectives for 1975: Research will be pursued aimed at synthesis and testing of contraceptive drugs, development of new methods of sterilization, and investigation of possible new ways to administer contraceptive drugs. The design and testing of reversible sterilization devices will also be an area of further exploitation. Continued efforts will be made regarding the evaluation of contraceptive methods. These will include the surveillance of women utilizing oral contraceptives, and study of the adverse medical events and long term complications with vasectomy, an increasingly popular method of male sterilization. Behavioral science research will initiate new investigations to study the social and psychological factors which determine effective contraceptive practice. Additional studies will deal with the consequences of population change, changing age distributions, and economic and environmental population factors. Research in the basic reproductive biology program will permit the continued development of fundamental biomedical research leads and the exploitation of some of these leads to obtain increased knowledge of fertility regulation and infertility problems.

NATIONAL INSTITUTES OF HEALTH

National Institute of Child Health and Human Development

Program Purpose and Accomplishments

Activity: Child Health (Public Health Service Act, Title IV, Part E)

1974			1975	
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
---	$51,992,000	Indefinite	---	$52,278,000

Purpose: The Child Health program encompasses research on the segment of the life span beginning with the moment of conception and extending through the later teenage years.

Explanation: Research includes the health of the mother; the effect of her health on the child; and the survival of the child through the hazards of intrauterine life, the birth process, and the adjustments to the new extrauterine environment. The focus then shifts to the study of nutritional, hormonal, social, psychological and other factors relating to the kind of adult the child will become. Research investigations include normal development of children and youth, abnormal development and mental retardation, and infant survival and well-being.

Accomplishments in 1974: The perinatal biology and infant mortality program accomplished research concerning the causes of maternal diseases and complications, low birth weight, fetal monitoring, and the sudden infant death syndrome (SIDS). The mental retardation program produced important results in a variety of areas including genetics, the treatment of metabolic diseases, and prenatal diagnosis. Accomplishments in the growth and development program were shown in immunology, growth hormone research, nutrition, and learning and communication.

Objectives for 1975: Continued emphasis will be given to research concerning low birth weight, maternal diseases and complications, prenatal and fetal diagnosis, and SIDS in the perinatal biology and infant mortality program. In addition, this program will increase its efforts in the psychosocial dynamics of pregnancy. The mental retardation program will continue in its many areas of scientific interest and provide additional emphasis in genetics, immunology, environmental factors, neurobiology, early diagnosis and intervention, and amelioration and treatment. The growth and development program will increase research efforts in adolescent development and continue endeavors concerning the susceptibility to disease, growth failure, nutrition, and communication.

NATIONAL INSTITUTES OF HEALTH

National Institute of Child Health and Human Development

Program Purpose and Accomplishments

Activity: Aging (Public Health Service Act, Title IV, Part E)

1974			1975	
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
---	$10,970,000	Indefinite	---	$9,078,000

Purpose: The aging program of the Institute is responsible for medical, biological, psychological, and social aspects of research relevant to the health of the elderly.

Explanation: The program supports research on the multitude of biological changes that occur with aging and are major determinants of disease processes, studies of cognitive and emotional alterations that occur with increasing age, and investigations of societal aspects of aging.

Accomplishments in 1974: The research on aging in women has recently concentrated on the study of the menopause. Research is continuing to determine the processes related to the menopause and any harmful long-term results of the treatment for the menopause. Because the age-structure has great implications for society a mathematical model is needed into which can be fed estimates of those rates for future years and data on the present population structure. The Institute is supporting studies of the currently existing models, and is investigating possible developments to increase their suitability to the task at hand. It has recently been discovered that there is a striking diminution in immunological competence with increasing age. Experimental animal studies are now underway to determine whether the immunologic deterioration that occurs with age involves changes in the function of individual cells, changes in the number of specific cells present, or changes in the microenvironment in which they operate. In the area of cellular aging, it has been found that normal human cells cannot live indefinitely in tissue culture although malignant ones can.

Objectives for 1975: The program on the treatment of the post-menopausal state will include retrospective and prospective investigations of hormonal treatment of that condition. More sophisticated models will be developed for the changing age-structure of the population. Projections of future population age-structures will be made and the implications of these for health and societal functions will be considered. Utilizing many of the known risk factors, the Institute plans to support the development and refinement of a system for individualized preventive medicine. Research on aging at the cellular and molecular levels will eventually open the doors to understanding the aging process of the organism as a whole. In 1975, investigations will continue in this area, including the cell's ability to reproduce itself. In the area of immunology and aging, studies of the effect of several variables on aging of the immune system will be continued, and established leads will be explored.

NATIONAL INSTITUTES OF HEALTH

National Institute of Child Health and Human Development

Program Purpose and Accomplishments

Activity: Intramural, Laboratory and Clinical Research (Public Health Service Act, Title IV, Part E)

1974		1975		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
338	$14,225,000	Indefinite	348	$14,727,000

Purpose: The Intramural, Laboratory and Clinical Research program comprises the Institute's intramural effort, including biometry and epidemiology, in the three major program areas of population and reproduction, child health and aging.

Explanation: The population and reproduction program includes research in reproductive biology, endocrinology, and ecology. The child health program includes research on maternal-child interactions, nutrition and development, behavioral and neurophysiological research, and biochemical aspects of development. The aging program, conducted at the Gerontology Research Center in Baltimore, includes research in cellular biology, biochemistry, physiology and psychological development.

Accomplishments in 1974: The ongoing mission in population research is the development of scientific data and theory basic to reproductive biology. To define the processes of fetal and early childhood development programs are being conducted in developmental biochemistry, neurophysiology, child psychology and environmental influences on childhood maturation. The processes of cellular and molecular aging continue to be investigated toward a greater understanding of mechanisms of the changes of aging.

The major projects underway in the Epidemiology Branch relate to various aspects of pregnancy, outcome of pregnancy and events occurring during the first year of life. The Biometry Branch is currently studying whether women who use steroid contraceptives have any ill effects in their future pregnancies.

Objectives for 1975: Continued efforts will be in the direction of strengthening the intramural effort in the area of reproductive biology. The intramural research program will expand in the area of perinatal biology research, to study the physiologic changes of pregnancy, delivery and adaptation of the newborn. Other programs will be continued in the areas of developmental immunology, neurophysiology, information transfer and acquisition. In aging research, continued emphasis will be given to the age-related changes in immunologic functions. The longitudinal study will analyze changes which characterize aging in contrast to changes resulting from disease.

The biometry and epidemiology endeavor will be continued. Studies will include a clinical trial to test the possible toxic effects and general effectiveness of phototherapy for high blood levels of bilirubin in newborns, and the epidemiology of the sudden infant death syndrome.

NATIONAL INSTITUTES OF HEALTH

National Institute of Child Health and Human Development

Program Purpose and Accomplishments

Activity: Research Management and Program Services (Public Health Service Act, Title IV, Part E)

1974		1975		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
181	$8,325,000	Indefinite	181	$8,532,000

Purpose: This activity supports: 1) the Director and his immediate staff concerned with administrative management, program planning and evaluation, and research information, 2) the scientific and administrative staff responsible for grant and contract programming, review and administration, 3) the scientific staff associated with the Center for Population Research, and 4) research conferences.

Explanation: This activity provides the funds for salaries and other related operating costs for the overall administration and direction of the programs of the Institute. Funds for the grant and contract programs are provided under the appropriate program.

Accomplishments in 1974: The staff supported by this activity continues to provide administrative management, program guidance and supportive services to the Institute's staff, in the furtherance of the Institute's programs to meet its goals. In 1974, it is estimated that 1,265 grants and 213 research contracts will be awarded. It is estimated that 20 research conferences will be held relating to the Institute's programs.

Objectives for 1975: This activity will continue to provide for the coordination, administration, and direction of the Institute's research programs. In 1975, it is estimated that 1,453 grants and 213 research contracts will be funded. The Institute plans include the continued support of the research conference program in 1975.

New Positions Requested

	1975		
	Grade	Number	Annual Salary
Intramural, laboratory and clinical research			
Medical Officer	GS-16	1	$ 32,806
Medical Officer	GS-14	1	24,247
Medical Officer	GS-13	3	62,031
Biologist	GS-9	1	12,167
Chemist	GS-7	2	19,938
Biologist	GS-5	1	8,055
Secretary	GS-5	1	8,055
Total new positions, all activities		10	167,299

Friday, March 29, 1974.

RESEARCH RESOURCES

WITNESSES

DR. THOMAS G. BOWERY, DIRECTOR

DR. ROBERT S. STONE, DIRECTOR, NATIONAL INSTITUTES OF HEALTH

DAVID L. CHICCHIRICHI, EXECUTIVE OFFICER, DIVISION OF RESEARCH RESOURCES

BERTIL G. BERGQUIST, BUDGET OFFICER, DIVISION OF RESEARCH RESOURCES

LELAND B. MAY, ACTING DIRECTOR OF FINANCIAL MANAGEMENT, NATIONAL INSTITUTES OF HEALTH

CHARLES MILLER, DEPUTY ASSISTANT SECRETARY, BUDGET

Object Classification (in thousands of dollars)

Identification code 09-25-0848-0-1-651		1973 actual	1974 est.	1975 est.
	Personnel compensation:			
11.1	Permanent positions	1,221	1,272	1,297
11.3	Positions other than permanent	52	58	60
11.5	Other personnel compensation	6	7	8
	Total personnel compensation	1,279	1,337	1,365
12.1	Personnel benefits: Civilian	144	150	151
21.0	Travel and transportation of persons	119	130	130
22.0	Transportation of things	4	5	5
23.0	Rent, communications, and utilities	95	102	114
24.0	Printing and reproduction	42	50	50
25.0	Other services	2,475	2,253	2,108
26.0	Supplies and materials	22	24	24
31.0	Equipment	14	15	15
41.0	Grants, subsidies, and contributions	68,654	125,065	78,738
99.0	Total obligations	72,846	129,131	82,700

Personnel Summary

Total number of permanent positions	77	72	72
Full-time equivalent of other positions	5	7	7
Average paid employment	81	77	77
Average GS grade	8.5	8.6	8.6
Average GS salary	$14,260	$15,138	$15,473
Average salary of ungraded positions	$11,138	$12,018	$12,253

Program and Financing (in thousands of dollars)

	Identification code 09–25–0848–0–1–651	1973 actual	1974 est.	1975 est.
	Program by activities:			
	1. Clinical research	48,623	42,531	42,485
	2. Biotechnology research	12,655	11,923	11,945
	3. Laboratory animal sciences and primate research	20,827	18,941	17,468
	4. General research support	---------	45,250	---------
	5. Minority biomedical support	---------	7,000	7,270
	6. Chemical biological information handling research	1,228	1,000	1,000
	7. Research management and program services	2,590	2,486	2,532
	Total program costs, funded [1]	85,923	129,131	82,700
	Change in selected resources (undelivered orders)	−13,077	---------	---------
10	Total obligations	72,846	129,131	82,700
	Financing:			
25	Unobligated balance lapsing	2,245	---------	---------
	Unobligated balance restored	---------	−2,196	---------
	Budget authority	**75,091**	**126,935**	**82,700**
	Budget authority:			
40	Appropriation	75,073	133,472	82,700
	Withheld from obligation and expenditure (Public Law 93–192)	---------	−5,153	---------
41	Transferred to other accounts	---------	−6	---------
42	Transferred from other accounts	18	---------	---------
43	**Appropriation (adjusted)**	**75,091**	**128,313**	**82,700**
45	**Proposed transfer for pay raises**	---------	**−1,378**	---------
	Relation of obligations to outlays:			
71	Obligations incurred, net	72,846	129,131	82,700
72	Obligated balance, start of year	50,225	49,392	99,915
73	Obligated balance transferred, net	---------	45,667	---------
74	Obligated balance, end of year	−49,392	−99,915	−41,198
77	Adjustments in expired accounts	−399	---------	---------
90	Outlays	73,280	124,275	141,417

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[1] Includes capital outlay as follows: 1973, $8 thousand; 1974, $14 thousand; 1975, $15 thousand.

Note.—Excludes $6 thousand in 1974 and 1975 for activities transferred to Departmental Management. Comparable amount for 1973 ($6 thousand) is included above.

WITNESS INTRODUCTION

Mr. **Flood**. Now we have research resources. The presentation will be made by Dr. Thomas G. Bowery.

We have a biographical sketch of you, Doctor, which we will print in the record.

[The biographical sketch follows:]

BIOGRAPHICAL SKETCH

Name: Thomas G. Bowery.

Position: Director, Division of Research Resources.

Birthplace and date: Bellevue, Pennsylvania, December 17, 1921.

Education: Michigan State University, 1943, B.S.; Rutgers University, 1948; M.S.; Rutgers University, 1951, Ph. D.

Experience: Present, Director, Division of Research Resources; 1968–1969, Acting Director, Division of Research Resources; 1967–1968, Associate Director for Operations, Division of Research Facilities and Resources, National Institutes of Health; 1965–1967, Assistant Chief for Operations, Division of Research Facilities and Resources, National Institutes of Health; 1964–1965, Extramural Operations and Procedures Officer, Office of the Director, NIH; 1963–1964, Special Assistant to the Associate Director for Research Grants, Office of the Director, NIH; 1962–1963, Grants Associate, Division of Research Grants, NIH; 1959–1962, Research Professor, Department of Entomology, North Carolina State College, Raleigh, N.C.; 1953–1959, Research Associate Professor, Department of Chemistry, North Carolina State College, Raleigh, N.C.; 1951–1952, Research Assistant Professor, Pesticide Residue Laboratory, Everglades Experiment Station, University of Florida, Belle Glade, Fla.; 1948–1951, Research Associate in Chemistry, Office of the State Chemist, New Jersey Agricultural Experiment Station, New Brunswick, N.J.; 1946–1948, Research Fellow, Entomology Department, Rutgers University, New Brunswick, N.J.

Association memberships: American Assiciation for the Advancement of Science; American Chemical Society, Sigma Xi.

Publications: Author of some 23 publications in seven journals.

Mr. **Flood**. Is there anybody you would like us to know?

Dr. **Bowery**. Mr. Chicchirichi, the Division's Executive Officer, and Mr. Bergquist, the Division's Budget Officer.

Mr. **Flood**. You have a prepared statement. What are you going to do with it?

Dr. **Bowery**. I would like to read it into the record, sir.

Mr. **Flood**. Please do.

OPENING STATEMENT

Dr. **Bowery**. Mr. Chairman and members of the committee. Thank you for once again extending an opportunity for me to speak to you about the programs of the Division of Research Resources. Each year, for a number of years, I have had the pleasure of describing the mission of the Division and of its several programs. Since most of you are fully aware of these missions, and since they are described in the narrative justification before you, they will not be repeated at this time. I will simply point out that the mission of the Division is pursued through six program activities: Clinical research, biotechnology research, chemical/biological information handling research, laboratory animal sciences and primate research, minority biomedical support, and general research support. I would now like to describe to you some of the scientific and administrative activities within these programs which have been designed to further their development as necessary, useful, and economically feasible resources for the Nation's biomedical research endeavors.

CLINICAL RESEARCH

The Division's clinical research program was initiated in 1960, and provides the resources through which the Nation's leading clinical investigators close the gaps in medical knowledge and translate the latest laboratory discoveries into improved treatment and care for patients.

During the period 1973 to 1974 the Division staff, together with outside consultants, conducted an intensive evaluation of this program. I am pleased to be able to report that the results of this evaluation have indicated that the objectives of the program are being met. I would now like to report on several of the most important of these objectives and illustrate the ways in which the programs has developed.

Through the continued support of 83 general clinical research centers in 76 institutions involving 890 research beds and amounting to 83 percent of NIH support for research patient care costs in 1973, the program is meeting its primary goal of increasing the total body of knowledge concerning the etiology, progression, prevention, control and cure of human disease through the direct study of physiology and pathophysiology in man.

The centers were designed as a resource to a medical institution permitting the enhancement of clinical investigation through the establishment of a discrete physical unit in the hospital but apart from the general care wards. They provide a stable, well trained, nursing and dietary staff needed for precise control and observation of the research subject. The research conducted in the facility derives its support from research grants from other NIH sources. In 1972, the latest year for which information is available, investigators conducting research in Division-supported general clinical research centers received $108 million in Federal research support mainly from the NIH categorical institutes.

The program is contributing to the maintenance of a pool of qualified clinical investigators by providing within the medical school and university-affiliated hospital settings, exposure of a large number of individuals to the clinical research process. Included among these are medical students, interns, residents, fellows, dietary interns, and nurses, as well as fully trained clinical investigators. In 1973 approximately 12,000 such individuals were involved in center activities.

The evaluation study indicated that the program should continue to be responsive to the shifting needs of clinical research by modification of program components as it has over the last several years.

BIOTECHNOLOGY RESEARCH

The biotechnology research program sponsors the development, use, and evaluation of health-relevant technologies such as digital computation, mass spectrometry, and high voltage electron microscopy. Biotechnology resources are centers of excellence through which concepts, tools, and methods of the physical sciences, mathematics, and engineering are brought to bear on biomedical problems. Being highly specialized and difficult to replicate but offering capabilities useful in almost any biomedical research setting, these resources increasingly must be viewed as regional or national centers available to qualified biomedical scientists outside the host institution as well as within.

We are making a special effort to promote the emergence and continuing development of shared biotechnology resources. This new program emphasis is designed to build on and to extend existing knowledge and resources, both by making specialized resources more readily available to the national scientific community and by linking resources together in networks that offer more nearly complete and effective research support than do their individual components. Through linking related but dissimilar research programs and technologies, new kinds and qualities of resources, not limited to the locally available talents and facilities, will be provided. By extending the availability of skills and facilities resident in single institutions, economies and increased effectiveness of Federal grant funds will be achieved.

The biotechnology research program now includes three high voltage electron microscope facilities, in which research opportunities are made available to qualified investigators throughout the United States under the guidance of a group of distinguished research leaders in high voltage electron microscopy.

The program also includes two research resources engaged in investigations of advanced computer science in medicine. These resources are being linked with one another and with collaborating scientists throughout the country via a digital telecommunication system.

Examples of other activities which appear appropriate for inclusion in the shared resource effort are other fields of biomedical computer research such as biomolecular modeling and chemical-biological information-handling systems and other kinds of biotechnology resources such as high resolution mass spectroscopy and nuclear magnetic resonance spectroscopy centers.

CHEMICAL BIOLOGICAL INFORMATION HANDLING

Some 5 years ago the division initiated a research and development activity focused on the design of an interactive computer tool for use by scientists involved in drug research. This unique and powerful system, called PROPHET, allows investigators who have little or no prior computer experience to use the computer remotely by way of a TV-like display terminal connected via telephone lines. In 1973 this activity reached an important milestone—it became fully operational and began serving 30 laboratory and clinical investigators at 4 geographically dispersed installations. This user community will be expanded by the end of 1974 to include approximately 65 investigators at 6 sites. An additional sizable number of users, approximately 35, will be added during 1975.

We are extremely pleased with the early success of this national resource. Because of the ease of accessibility and the resource's ability to handles a large volume of complex research interactions, it appears to be an extremely cost-effective and efficient way of conducting pharmacological research and facilitating scientific communication.

CLINICAL-BIOTECHNOLOGY COLLABORATION

During 1973 the Division initiated, through its clinical research and biotechnology research programs, an inquiry into the processes involved in the collection and analyses of clinical research information. This inquiry is aimed at the identification and characterization of intellectual tasks and the information flows in clinical investigation and the development of methods for facilitating this process. The project utilizes existing clinical research centers, supported by the Division, where much of the Nation's clinical research is being conducted.

The results of the inquiry to date indicate that the facilities currently available to clinical investigators for data organization, storage, retrieval, and analysis are inadequate. They further indicate that clinical research could be greatly facilitated if investigators had available to them readily accessible, local, economical, convenient-to-use data collection and data management systems. Specifications for such a system were recently completed and we are encouraged by its potential for enchancing clinical research.

LABORATORY ANIMAL AND PRIMATE RESEARCH

One of the major concerns in the field of animal research is the increasing scarcity of subhuman primates. Always a problem, this is becoming much more acute because India, which has historically provided many of the primates used in the United States, has drastically reduced the number of primates it will allow to be exported. Since, at the present time, only about 5 percent of the 60,000 primates used annually in the United States are bred domestically, the reduction in the number imported from India will obviously become a serious problem.

To counteract this problem the laboratory animal sciences and primate research program of the Division is engaged in a number of activities aimed at increasing the number of domestically bred animals. The first step is to increase primate breeding programs in the existing NIH-supported primate centers, including the one at the Caribbean Primate Research Center located at Sabana Seca, P.R. Second, we have used the research contract mechanism to study the feasibility of the commercial breeding of primates within the United States. In addition. other foreign sources of wild caught primates will be investigated and some research studies currently utilizing primates will be modified so that other nonprimate species can be used.

I am pleased to report significant progress in helping institutions improve their animal care programs to meet the standards of the Animal Welfare Act of 1970, Public Law 89–544, and the Department of Health, Education, and Welfare policy on the care and use of animals. The initiative was launched 3 years ago and has helped 62 institutions provide better care for the animals required in research programs. We estimate that if a similar number of institutions are assisted over the next 3 years this initiative will have achieved its basic objective.

MINORITY BIOMEDICAL SUPPORT

In 1972 the Division initiated a program which was designed to bring minority students, faculty and institutions into a more competitive and productive position relative to the biomedical research field. I am pleased to state that as this competitive research grant program nears the completion of its third year, progress is being made toward the increased involvement of minorities in health research. During the first 2 years of the program 398 faculty, 648 undergraduate, and 115 graduate students received support for their research and research training activities. It is anticipated that the final results of the fiscal year 1974 support will increase this figure by approximately 20 percent. This represents a significant increase in the involvement of minorities in this field since the establishment of the minority biomedical support program.

Despite this early success there are significant numbers of minorities interested in biomedical research careers which are not being served. To remedy this situation the MBS program is being modified and is now open to the following groups of institutions: (a) Native American Indian Reservations; (b) 2-year and 4-year colleges, universities, and health professional schools in which student enrollments are drawn mainly from ethnic minority groups (such as Blacks, Spanish-speaking Americans, American Indians, Orientals, and Polynesians, et cetera), and (c) academic institutions with significant, but less than 50 percent, ethnic minority enrollments, provided they have a demonstrated commitment to special encouragement for the advancement of minority students, they have a historic role of established interest in such students, and they are in geographic proximity to ethnic minority populations.

GENERAL RESEARCH SUPPORT

The narrative justification before you requests no funds for the "formula-award" elements of the general research support program in fiscal year 1975. This was based on the decision that these institutional formula awards, which were designed to provide untargeted research funds to institutions to strengthen their biomedical research capacity, are now of a lower priority than are program oriented research project activities.

BUDGET

Mr. Chairman, the budget request for 1975 is $82,700,000. I shall be pleased to try to answer any questions and supply additional information desired for the record.

BUDGET REQUEST

Mr. Flood. Doctor, you said your budget request for 1975 is $82.7 million. That is a reduction of $44.2 million from the 1974 adjusted appropriation level, isn't it?

Dr. Bowery. That is correct.

Mr. Flood. That is major surgery, isn't it? One lung anyhow. Well, you are breathing.

The area in which you are proposing to make this reduction is the general research support grants. Right?

Dr. Bowery. That is correct.

Mr. Flood. You received $36.8 million in restored 1973 funds in fiscal year 1974. Was all of that money invested in general research support grants?

Dr. Bowery. All except about $2.2 million.

MULTIYEAR GRANT AWARDS

Mr. Flood. Did you make any multiyear grant awards in 1974 for general research support grants?

Dr. Bowery. No, we made no multiyear awards. We can indicate the amount made available in 1974 which included some of the released unobligated balances from 1973.

Mr. Flood. We want a list of that and the amounts.

[The information follows:]

General Research Support Program

General Research Support Grant Awards

FY 1973 Restored and FY 1974 Awards*

Name of Institution	1973 Restored	1974* Award	Total Awarded
University of Alabama, Birmingham - Dental	$145,887	$150,966	$296,853
University of Southern California, L.A. - Dental	43,193	53,237	96,430
University of California, L.A. - Dental	86,668	78,264	164,932
University of California, S.F. - Dental	44,428	54,569	98,997
Georgetown University, D.C. - Dental	17,030	0	17,030
Emory University, Atlanta - Dental	54,323	43,583	97,906
University of Illinois, Chicago - Dental	30,728	26,307	57,035
Northwestern University, Chicago - Dental	13,506	0	13,506
Indiana University, Indianapolis - Dental	15,909	29,715	45,624
University of Iowa, Iowa City - Dental	99,446	114,996	214,442
University of Kentucky, Lexington - Dental	13,887	18,330	32,217
University of Louisville - Dental	15,162	0	15,162
University of Maryland, Baltimore - Dental	13,915	0	13,915
Harvard University, Boston - Dental	75,995	83,789	159,784
Tufts University, Boston - Dental	22,517	26,833	49,350
University of Michigan, Ann Arbor - Dental	128,984	153,876	282,860
University of Minnesota, Minneapolis - Dental	78,318	89,805	168,123
University of Missouri, Kansas City - Dental	24,772	32,754	57,526
State University, N.Y. Buffalo - Dental	27,229	29,992	57,221
Columbia University, New York - Dental	66,446	70,138	136,584
New York University, New York - Dental	36,373	35,025	71,398
University of North Carolina, Chapel Hill - Dental	117,913	128,250	246,163
Case Western Reserve University, Cleveland - Dental	30,287	33,239	63,526
University of Oregon, Portland - Dental	32,114	30,143	62,257
University of Pennsylvania, Philadelphia - Dental	108,921	129,125	238,046
University of Pittsburgh - Dental	27,971	30,736	58,707
University of Texas Health Science Center, Houston-Dental	73,779	87,165	160,944
University of Washington, Seattle - Dental	20,686	31,207	51,893
West Virginia University, Morgantown - Dental	15,166	18,104	33,270
University of Alabama, Birmingham - Medical	204,090	252,822	456,912
University of Arkansas, Little Rock - Medical	104,820	92,841	197,661
University of California, Irvine - Medical	80,955	118,598	199,553
Loma Linda University - Medical	56,113	67,580	123,693
Stanford University, Stanford - Medical	225,661	252,822	478,483
University of California, L.A. - Medical	225,661	252,822	478,483
University of California, S.F. - Medical	225,661	252,822	478,483
University of Southern California, L.A. - Medical	184,821	252,822	437,643
University of Colorado, Denver - Medical	225,661	252,822	478,483

Name of Institution	1973 Restored	1974* Award	Total Awarded
Yale University, New Haven - Medical	$225,661	$252,822	$478,483
George Washington University, D.C. - Medical	104,447	132,044	236,491
Georgetown University, D.C. - Medical	141,261	142,818	284,079
Howard University, D.C. - Medical	93,434	128,731	222,165
University of Florida, Gainesville - Medical	170,900	182,181	353,081
University of Miami - Medical	223,942	252,822	476,764
Emory University, Atlanta - Medical	166,918	196,344	363,262
Medical College of Georgia, Augusta	104,202	116,312	220,514
Chicago Medical School/University of Health Sciencs	41,745	45,705	87,450
University of Chicago, Pritzker School of Medicine	225,661	252,822	478,483
Loyola University, Stritch School Medical, Maywood	75,239	98,748	173,987
University of Illinois, Chicago - Medical	157,735	175,983	333,718
Northwestern University, Chicago - Medical	167,623	203,023	370,646
Indiana University, Indianapolis - Medical	168,309	196,705	365,014
University of Iowa, Iowa City - Medical	209,786	252,822	462,608
University of Kansas, Kansas City - Medical	146,895	164,322	311,217
University of Kentucky, Lexington - Medical	99,288	80,865	180,153
University of Louisville - Medical	71,783	82,182	153,965
Louisiana State University, New Orleans - Medical	106,181	140,459	246,640
Tulane University, New Orleans - Medical	157,914	180,732	338,646
Johns Hopkins University, Baltimore - Medical	225,661	252,822	478,483
University of Maryland, Baltimore - Medical	159,306	170,681	329,987
Boston University, Boston - Medical	194,418	235,167	429,585
Harvard University, Boston - Medical	225,661	252,822	478,483
Tufts University, Boston - Medical	143,004	193,167	336,171
University of Michigan, Ann Arbor - Medical	225,661	252,822	478,483
Wayne State University, Detroit - Medical	120,157	160,508	280,665
University of Minnesota, Minneapolis - Medical	225,661	252,822	478,483
University of Mississippi, Jackson - Medical	135,424	142,175	277,599
University of Missouri, Columbia - Medical	145,091	164,303	309,394
Saint Louis University - Medical	143,847	156,223	300,070
Washington University, Saint Louis - Medical	225,661	252,822	478,483
Creighton University, Omaha - Medical	27,860	39,522	67,382
University of Nebraska, Omaha - Medical	77,521	93,777	171,298
Dartmouth College, Hanover - Medical	143,774	159,110	302,884
NJ Medical School-College of Medical & Dental - Newark	88,256	107,203	195,459
Albany Medical College of Union University	139,457	172,261	311,718
Columbia University, New York - Medical	225,661	252,822	478,483
Cornell University, New York - Medical	194,513	244,585	439,098
Yeshiva Univ., A. Einstein College - Medical, Bronx	225,661	252,822	478,483
New York Medical College, New York	152,819	165,433	318,252
New York University, New York - Medical	225,661	252,822	478,483
State University of New York, Buffalo - Medical	191,369	202,567	393,936
State University of New York, Downstate, Brooklyn - Med.	170,140	190,758	360,898
State University of NewYork, Upstate, Syracuse - Medical	140,384	156,323	296,707

Name of Institution	1973 Restored	1974* Award	Total Awarded
University of Rochester - Medical	$220,404	$252,822	$473,226
Wake Forest U. Bowman Gray School of Med.	135,449	167,820	303,269
Duke University, Durham - Medical	225,661	252,822	478,483
U. of North Carolina, Chapel Hill - Medical	216,602	246,169	462,771
U. of North Dakota, Grand Forks - Medical	35,153	23,836	58,989
University of Cincinnati - Medical	162,118	187,981	350,099
Ohio State University, Columbus - Medical	152,517	170,632	323,149
Case Western Reserve U., Cleveland - Medical	214,382	242,516	456,898
Univ. of Oklahoma, Oklahoma City - Medical	100,204	151,416	251,620
University of Oregon, Portland - Medical	167,598	194,675	362,273
Hahnemann Medical College & Hospital, Phila.	96,151	122,165	218,316
Jefferson Med. College of T J University - Phila.	154,987	176,145	331,132
University of Pennsylvania, Philadelphia - Medical	225,661	252,822	478,483
University of Pittsburgh - Medical	187,878	200,909	388,787
Temple University, Philadelphia - Medical	217,614	251,772	469,386
Medical College of Pennsylvania - Philadelphia	58,401	91,402	149,803
University of Puerto Rico, San Juan - Medical	83,327	102,332	185,659
Med. U. of South Carolina, Charleston	78,147	126,635	204,782
University of South Dakota, Vermillion - Medical	24,010	18,634	42,644
Meharry Medical College, Nashville - Medical	45,682	68,181	113,863
University of Tennessee, Memphis - Medical	149,401	173,362	322,763
Vanderbilt University, Nashville - Medical	225,661	252,822	478,483
Baylor College of Medicine - Houston	225,661	252,822	478,483
Univ. of Texas, SW Medical School, Dallas	217,432	252,822	470,254
Univ. of Texas, Med. Br., Galveston	154,019	177,347	331,366
University of Utah, Salt Lake - Medical	185,027	210,383	395,410
University of Vermont, Burlington - Medical	144,293	160,082	304,375
Va. Comm. U. Med. Col. of Va., Richmond - Medical	153,803	209,729	363,532
University of Virginia, Charlottesville - Medical	154,257	172,496	326,753
University of Washington, Seattle - Medical	225,661	252,822	478,483
West Virginia University, Morgantown - Medical	45,217	55,296	100,513
University of Wisconsin, Madison - Medical	225,661	252,822	478,483
University of California, Berkeley - Pub. Health	104,032	114,345	218,377
University of California, L.A. Pub. Health	40,007	67,497	107,504
Yale University, New Haven - Public Health	106,544	109,313	215,857
Tulane University, New Orleans - Public Health	38,115	41,252	79,367
Johns Hopkins University, Baltimore - Public Health	169,678	203,433	373,111
Harvard University, Boston - Public Health	165,417	202,508	367,925
University of Michigan, Ann Arbor - Public Health	121,425	134,228	255,653
University of Minnesota, Minneapolis - Public Health	25,470	15,665	41,135
Columbia University, N.Y. - Public Health	102,271	103,741	206,012
University of North Carolina, Chapel Hill - Public Health	52,542	41,757	94,299
University of Pittsburgh - Public Health	29,219	36,896	66,115
University of California, S. F. Pharmacy	68,580	89,497	158,077
The Medical College of Wisconsin, Inc.	138,518	171,282	309,800

Name of Institution	1973 Restored	1974* Award	Total Awarded
State U. N. Y., Buffalo - Pharmacy	$73,335	$63,927	$137,262
University of Pittsburgh - Pharmacy	41,905	20,065	61,970
Univ. of Wisconsin, Madison - Pharmacy	41,502	44,911	86,413
University of California, Davis - Vet.	81,258	78,628	159,886
Colorado St. Univ., Ft. Collins - Vet.	61,123	67,998	129,121
Purdue University, W. Lafayette - Vet.	29,532	22,546	52,078
University of Illinois, Urbana - Vet.	23,811	27,059	50,870
Univ. of Minnesota, St. Paul - Vet.	19,960	0	19,960
N. Y. St. Vet. Col. at Cornell U., Ithaca	74,262	74,006	148,268
Ohio State University, Columbus - Vet.	27,096	27,363	54,459
Univ. of Pennsylvania, Phila. - Vet.	111,769	141,798	253,567
Washington State Univ., Pullman - Vet.	28,573	39,420	67,993
Pro. Staff Assoc. LAC/USC Med. Ctr.	30,605	52,658	83,263
Childrens Hosp. Med. Center, Oakland	23,720	38,233	61,953
Cedars-Sinai Medical Ctr., L. A. - Hosp.	78,673	102,810	181,483
Childrens Hospital of Los Angeles	104,537	112,872	217,409
City of Hope Nat. Med. Ctr. Duarte - Hosp.	137,483	161,572	299,055
Mount Zion Hosp. and Med. Center, S. F.	49,010	74,573	123,583
National Jewish Hospital at Denver	63,171	89,290	152,461
Childrens Memorial Hospital, Chicago	67,983	63,524	131,507
Michael Reese Hosp. and Med. Ctr., Chicago	65,218	96,916	162,134
Rush-Pres-St. Lukes Med. Ctr., Chicago - Hosp.	123,154	127,651	250,805
Beth Israel Hospital, Boston	120,419	137,611	258,030
Childrens Hosp. Med. Ctr., Boston	187,057	226,688	413,745
Forsyth Dent. Inf. for Children, Boston	120,148	125,158	245,306
McLean Hospital, Belmont	40,630	47,322	87,952
Mass. Eye and Ear Infirmary, Boston	80,296	49,167	129,463
Massachusetts General Hosp., Boston	225,661	252,822	478,483
University Hospital, Inc., Boston	132,765	153,524	286,289
Peter Bent Brigham Hospital, Boston	101,282	131,507	232,789
Henry Ford Hospital, Detroit	38,712	43,409	82,121
Jewish Hospital of St. Louis	54,486	71,705	126,191
Childrens Hospital of Buffalo	65,467	76,303	141,770
Hospital for Special Surgery, N. Y.	59,117	71,435	130,552
L. I. Jewish-Hillside Med. Ctr.	48,654	73,678	122,332
Maimonides Medical Center, Brooklyn	24,536	34,364	58,900
Montefiore Hosp. and Med. Ctr., Bronx	169,254	192,846	362,100
St. Lukes Hospital Center, New York	82,659	108,734	191,393
St. Vincents Hosp. and Med. Ctr. of N. Y.	28,633	31,097	59,730
Jewish Hosp. and Med. Ctr. of Brooklyn	21,643	21,805	43,448
Childrens Hospital, Columbus	30,858	0	30,858
Albert Einstein Med. Center, Phila.	58,777	57,017	115,794
Childrens Hospital of Philadelphia	97,613	135,229	232,842
Childrens Hospital of Pittsburgh	54,564	71,143	125,707
Philadelphia General Hospital	120,709	147,169	267,878

Name of Institution	1973 Restored	1974* Award	Total Awarded
Wills Eye Hospital, Philadelphia	$50,477	$55,248	$105,725
U. Texas, MD Anderson Hosp. and Tum., Houston	197,306	244,834	442,140
Palo Alto Medical Research Fdn.	34,493	46,561	81,054
Scripps Clinic and Res. Fdn., La Jolla	155,122	201,648	356,770
Res. Fdn., Childrens Hosp. of D. C.	102,862	136,478	239,340
Menninger Foundation, Topeka	31,267	33,715	64,982
Alton Ochsner Med. Fdn., New Orleans	24,606	30,224	54,830
Southwest Fdn. for Res. and Ed., S. A.	106,008	86,216	192,224
Pacific Northwest Res. Fdn., Seattle	34,666	66,296	100,962
Kaiser Foundation Hospitals, Oakland	14,975	25,141	40,116
Stanford Research Inst., Menlo Park	131,781	130,935	262,716
Child. Asthma Res. Inst. and Hosp., Denver	26,314	25,887	52,201
Hektoen I. Med. Res. of Cook Co., Chicago	27,375	32,380	59,755
Bio-Research Inst., Inc., Cambridge	24,927	35,843	60,770
Childrens Cancer Res. Fdn., Boston	149,811	173,260	323,071
Retina Foundation, Boston	77,496	88,069	165,565
Worcester Fdn. Exper. Biol., Shrewsbury	140,564	157,362	297,926
Michigan Cancer Foundation, Detroit	66,046	68,960	135,006
Mayo Foundation, Rochester, Minn.	219,314	252,822	472,136
Public Health Research Inst., N. Y.	119,269	128,236	247,505
Childrens Hospital, Cincinnati	112,368	136,354	248,722
Fels Research Inst., Yellow Springs	47,036	45,935	92,971
Oklahoma Med. Res. Fdn., Oklahoma City	105,166	87,218	192,384
Institute for Cancer Research, Philadelphia	177,944	205,763	383,707
Wistar Inst. of Anat. and Biol., Philadelphia	142,764	168,968	311,732
U. of Tenn. Mem. Res. Ctr. and Hosp., Knox.	39,605	60,205	99,810
A. S. A. Rancho L. Amigos Hosp., Downey	32,497	82,698	115,195
Jackson Laboratory, Bar Harbor	115,071	137,440	252,511
Friends Med. Sci. Research Center, Inc.	101,223	60,585	161,808
Eastman Dental Center, Rochester, N. Y.	29,412	42,045	71,457
Calif. St. Dept. of Pub. Health., Berkeley	49,992	40,005	89,997
Langley Porter Neuropsych. Inst., S. F.	85,569	0	85,569
A.S.A. Harbor Gen. Hospital, Torrance	134,223	158,598	292,821
Div. Health Dept. Health and Rehab. Ser. St. Fla.	43,598	49,544	93,142
Mass. Mental Health Res. Corp., Boston	30,249	37,320	67,569
Baltimore City Hospitals	34,477	22,672	57,149
Univ. of Illinois, Chicago - Pharmacy	14,634	0	14,634
Iowa State University, Ames - Vet.	35,302	33,432	68,734
Institute of Medical Sciences, S. F.	133,421	154,810	288,231
Oklahoma St. Univ., Stillwater - Vet.	27,972	38,593	66,565
Boston City Hospital	73,000	113,504	186,504
Magee-Womens Hospital, Pittsburgh	27,617	36,818	64,435
Univ. of Michigan, Ann Arbor - Pharmacy	26,980	33,341	60,321
Tuskegee Inst., Sch. Vet. Medicine	22,239	44,403	66,642
St. Josephs Hospital, Phoenix	24,866	39,102	63,968

Name of Institution	1973 Restored	1974* Award	Total Awarded
Rutgers, State University, Piscat. - Med.	$94,703	$116,896	$211,599
Inst. for Muscle Disease, Inc., N. Y.	33,515	29,817	63,332
Institute for Med. Research, Camden	50,790	57,010	107,800
U. of New Mexico, Albuquerque - Med.	83,045	139,121	222,166
St. Jude Childrens Res. Hosp., Memphis	130,229	150,251	280,480
Lankenau Hospital, Philadelphia	23,600	0	23,600
Purdue University, Lafayette	39,002	54,576	93,578
St. Elixabeth Hospital, Brighton	21,446	28,950	50,396
VA. Mason Fdn. Med. Ed. and Res., Seattle	36,045	28,464	64,509
Hosp. for Joint Dis. and Med. Ctr., N. Y.	46,803	83,023	129,826
Pennsylvania Hospital, Philadelphia	26,998	28,424	55,422
New England Deaconess Hosp., Boston	50,182	57,078	107,260
Montefiore Hosp. Assoc. W. Pa., Pitts.	20,502	16,642	37,144
Good Samaritan Hosp. and Med. Ctr., Port.	23,958	25,861	49,819
U. of Mississippi, University - Pharmacy	12,701	36,410	49,111
Salk Inst. for Biol. Studies, San Diego	117,841	139,127	256,968
Haskins Laboratories, Inc., New Haven	64,903	59,325	124,228
New England Med. Ctr. Hosps., Boston	164,029	190,376	354,405
University of Hawaii, Honolulu - Med.	112,242	129,130	241,372
University of Georgia, Athens - Vet.	21,635	17,113	38,748
Univ. of Missouri, Columbia - Vet.	54,850	54,663	109,513
University of California, S. F. - Nursing	39,662	22,673	62,335
University of Kansas, Lawrence - Pharmacy	29,179	27,204	56,383
Ohio State University, Columbus - Pharmacy	30,278	39,606	69,884
St. Margarets Hospital, Boston	21,311	0	21,311
Sonoma State Hospital, Eldridge	35,970	0	35,970
Presby. Univ. of Pa. Med. Ctr., Phila.	36,867	78,383	115,250
Home for Jewish Aged, Philadelphia	45,605	23,733	69,338
Oregon Research Institute, Eugene	78,493	93,684	172,177
Amer. Inst. for Res. Behav. Sci., Pitts.	54,842	34,009	88,851
Cancer Research Center, Columbia	31,174	60,780	91,954
New York Botanical Garden, Bronx	25,615	34,288	59,903
Michigan State Univ., E. Lansing - Vet.	42,623	48,480	91,103
St. Christophers H. for Child., Phila.	52,675	35,960	88,635
Blood Research Institute. Inc., Boston	17,751	19,527	37,278
Texas Res. Inst. Mental Sci., Houston	33,484	17,946	51,430
Evanston Hospital, Illinois	0	30,564	30,564
St. Vincents Charity Hospital, Cleveland	17,215	0	17,215
Pacific State Hospital, Pomona	59,446	0	59,446
University of Minnesota, Minneapolis - Pharmacy	22,806	31,225	54,031
Inst. for Behavioral Res., Sil. Spg.	69,095	63,733	132,828
Sinai Hospital of Detroit	56,126	68,124	124,250
St. Lukes Hospital, Cleveland	21,237	30,258	51,495
Roswell Park Memorial Inst., Buffalo	207,757	252,822	460,579
N. Y. St. Health Dept. Div. Lab. and Res., Albany	59,050	80,115	139,165

Name of Institution	1973 Restored	1974* Award	Total Awarded
N. Y. St. Psychiatric Institute, N. Y.	$114,851	$105,196	$220,047
Rockland State Hospital, Orangeburg	131,412	116,357	247,769
Mt. Sinai Sch. of Med. City U. of N. Y.	225,661	252,822	478,483
U. of Texas Med. Sch., San Antonio	91,734	97,214	188,948
Child. Ortho. Hosp. and Med. Ctr., Seattle	23,267	31,622	54,889
Michigan State Univ., E. Lansing - Med.	109,083	124,968	234,051
St. Joseph Hospital, Lancaster	23,499	0	23,499
Mt. Sinai Hospital of Cleveland	36,616	42,621	79,237
Mt. Sinai Hosp. of Gtr. Miami, Inc.	24,917	35,495	60,412
Roosevelt Hospital, New York	68,384	36,421	104,805
Brown University, Providence - Med.	113,884	128,181	242,065
Univ. of California, San Diego - Med.	225,661	252,822	478,483
Robert B. Brigham Hospital, Boston	67,732	74,209	141,941
Midwest Research Institute, Kansas City	22,434	17,292	39,726
Joslin Diabetes Fdn., Inc., Boston	63,434	74,360	137,794
Cleveland Clinic Foundation	63,127	98,696	161,823
University of Arizona, Tucson - Med.	126,040	160,506	286,546
University of Connecticut, Farm. - Den.	84,296	89,372	173,668
University of Connecticut, Farm. - Med.	76,741	116,838	193,579
Royce Thompson I. for Plant Res., N. Y.	27,704	20,112	47,816
Pennsylvania State Univ., Hershey - Med.	131,952	163,137	295,089
National Biomedical Res. Fdn., D. C.	33,432	18,154	51,586
University of California, Davis - Med.	141,581	141,199	282,780
New York Blood Center, New York	133,277	157,188	290,465
Amer. Dental Association, Chicago	53,622	68,670	122,292
Papanicolaou Cancer Research Inst.	30,248	48,658	78,906
John B. Pierce Fdn. Conn. Inc. New Haven	44,741	56,555	101,296
Medical Research Fdn. of Oregon, Port.	95,869	189,102	284,971
Va. Comm. U., Med. Col. of Va. - Pharmacy	25,955	29,398	55,353
Eye Research Foundation of Bethesda	31,664	34,736	66,400
Medical College of Ohio at Toledo	40,968	45,261	86,229
Univ. of Tennessee, Memphis - Pharmacy	24,239	0	24,239
Boston Univ., School of Grad. Dent.	26,644	30,994	57,638
Louisiana State University - Dental	23,070	16,232	39,302
Trudeau Institute, Inc., Saranac Lake	46,412	49,405	95,817
Mercy Catholic Med. Ctr. SE. Pa., Darby	22,791	32,524	55,315
Allegheny General Hospital, Pitts.	47,050	55,196	102,246
The Rand Corporation, Santa Monica	36,343	45,319	81,662
Boston Biomedical Research Inst. Inc.	103,806	116,219	220,025
Univ. of Massachusetts, Worcester - Med.	24,307	42,421	66,728
University of Washington - Pub. Health	72,953	68,759	141,712
Medical Foundation of Buffalo	33,471	54,159	87,630
Cold Spring Harbor Laboratory, N. Y.	115,839	134,185	250,024
Wayne State Univ. Col. of Nur., Detroit	30,015	28,736	58,751
Inst. for Res. in Soc. Behav., Berkeley	34,809	48,271	83,080

Name of Institution	1973 Restored	1974* Award	Total Awarded
Battelle Memorial Inst. Columbus Lab.	$72,927	$65,487	$138,414
Va. Comm. U., Med. College of Va., Rich - Dental	22,757	41,484	64,241
Univ. of Florida, Col. of Dental - Gaines.	14,687	40,294	54,981
Eunice K. Shriver Ment. Retard. Waltham	104,165	127,908	232,073
Assoc. Univ. Inc. Brook. Nat. Lab. Upton	38,264	80,053	118,317
Child Res. Center of Michigan, Detroit	36,006	22,032	58,038
State Univ. of New York, Stonybrook - Medical	24,298	31,673	55,971
American National Red Cross, D.C.	42,000	39,732	81,732
University of Utah, Salt Lake - Phar	18,802	29,286	48,088
Center for Policy Research, Inc. N.Y.	28,381	60,391	88,772
American Fdn. for Bio. Res., Madison	18,034	14,433	32,467
Ohio State Univ. School of Nursing, Col.	24,735	22,032	46,767
Univ. of Texas Med. School, Houston, Texas	51,452	71,090	122,542
Oak Ridge Associated Univ. Oak Ridge	42,031	33,267	75,298
University of Florida, Gainesville - A. H.	25,279	17,377	42,656
Mental Health Res. Unit N.Y. Dept. Mntl Hyg.	29,248	26,518	55,766
University of S. Florida, Tampa - Medical	18,183	41,841	60,024
Northwestern Memorial Hospital - Chicago	31,018	25,986	57,004
Mem. Hosp. for Cancer and Allied Dis.	117,989	185,468	303,457
U. of California Langley Porter Neuro Inst.	0	124,360	124,360
U. of California Neuropsychiatric Inst. L.A.	0	176,746	176,746
Totals as of April 5, 1974	29,043,000	33,486,217	62,529,217

*The balance of $4,739,000 will be awarded during the remainder of FY 1974.

Biomedical Sciences Support Grant Awards

FY 1973 Restored and FY 1974 Awards*

Name of Institution	1973 Restored	1974* Award	Total Awarded
University of Alaska, Fairbanks	$30,132	0	$30,132
University of Arizona, Tucson	27,713	0	27,713
Calif. Inst. of Technology, Pasadena	75,439	0	75,439
Stanford University, Stanford	65,187	0	65,187
University of California, Berkeley	139,092	0	139,092
University of California, Davis	54,517	0	54,517
University of California, Irvine	40,454	0	40,454
University of California, Los Angeles	64,915	0	64,915
University of California, Riverside	34,493	0	34,493
University of California, San Diego	68,877	0	68,877
University of Southern California, Los Angeles	44,643	0	44,643
University of Colorado, Boulder	46,428	0	46,428
University of Connecticut, Storrs	45,147	0	45,147
Yale University, New Haven	57,300	0	57,300
George Washington University, D. C.	18,063	0	18,063
Florida State University, Tallahassee	39,682	0	39,682
University of Florida, Gainesville	43,554	0	43,554
Emory University, Atlanta	24,119	0	24,119
Georgia Inst. of Technology, Atlanta	26,769	0	26,769
University of Georgia, Athens	40,208	0	40,208
University of Hawaii, Honolulu	38,650	0	38,650
Illinois Institute of Technology, Chicago	18,961	0	18,961
Northwestern University, Evanston	56,088	0	56,088
University of Chicago, Chicago	33,309	0	33,309
University of Illinois, Urbana	69,706	0	69,706
Indiana University, Bloomington	53,433	0	53,433
Purdue University, Lafayette	60,275	0	60,275
University of Notre Dame, Notre Dame	33,674	0	33,674
Iowa State Univ. of Sci. and Tech., Ames	34,155	0	34,155
University of Iowa, Iowa City	32,150	0	32,150
Kansas State University, Manhattan	26,885	0	26,885
University of Kansas, Lawrence	59,428	0	59,428
Tulane University, New Orleans	24,406	0	24,406
Johns Hopkins University, Baltimore	48,434	0	48,434
University of Maryland, College Park	29,186	0	29,186
Boston University, Boston	21,623	0	21,623
Brandeis Bniversity, Waltham	45,088	0	45,088
Harvard University, Cambridge	67,507	0	67,507

Name of Institution	1973 Restored	1974* Award	Total Awarded
Massachusetts Institute of Technology, Cambridge	$129,481	0	$129,481
University of Massachusetts, Amherst	40,467	0	40,467
Michigan State University., East Lansing	41,410	0	41,410
University of Michigan, Ann Arbor	62,847	0	62,847
Wayne State University, Detroit	33,626	0	33,626
University of Minnesota, Minneapolis	64,235	0	64,235
University of Missouri, Columbia	20,269	0	20,269
Washington University, St. Louis	54,293	0	54,293
University of Nebraska, Lincoln	20,504	0	20,504
Princeton University, Princeton	49,652	0	49,652
Rutgers, State University, New Brunswick	58,673	0	58,673
Rutgers, State University, Newark	32,250	0	32,250
Columbia University, New York	65,080	0	65,080
Cornell University, Ithaca	72,433	0	72,433
New York University, New York	37,677	0	37,677
Polytechnic Institute of Brooklyn, Brooklyn	24,711	0	24,711
Queens College, City University of New York, Flushing	19,685	0	19,685
Rockefeller University, New York	118,177	0	118,177
State University of New York, Buffalo	34,346	0	34,346
State University New York, Stony Brook	34,651	0	34,651
Syracuse University, Syracuse	35,034	0	35,034
University of Rochester, Rochester	35,929	0	35,929
Duke University, Durham	36,677	0	36,677
North Carolina State University, Raleigh	44,062	0	44,062
University of North Carolina, Chapel Hill	37,291	0	37,291
Ohio State University, Columbus	39,422	0	39,422
Oklahoma St. U. Agri. and Appl. Sci., Stillwater	24,363	0	24,363
Oregon State University, Corvallis	49,968	0	49,968
University of Oregon, Eugene	47,579	0	47,579
Carnegie Mellon University, Pittsburgh	35,357	0	35,357
Pennsylvania State U., Univ. Park	42,804	0	42,804
Univ. of Pennsylvania, Philadelphia	45,557	0	45,557
University of Pittsburgh, Pittsburgh	45,581	0	45,581
Brown University, Providence	36,251	0	36,251
Geo. Peabody Col. for Teachers, Nashville	35,899	0	35,899
University of Tennessee, Knoxville	25,827	0	25,827
Vanderbilt University, Nashville	31,043	0	31,043
Texas A & M University, College Station	25,473	0	25,473
University of Texas, Austin	56,618	0	56,618
University of Utah, Salt Lake City	43,234	0	43,234
Utah State University, Logan	19,784	0	19,784
University of Virginia, Charlottesville	40,060	0	40,060
Virginia Polytechnic Inst. and State U.	30,195	0	30,195
University of Washington, Seattle	71,411	0	71,411
Washington State Univ., Pullman	34,470	0	34,470

Name of Institution	1973 Restored	1974* Award	Total Awarded
University of Wisconsin, Madison	$95,194	0	$95,194
University of California, Santa Barbara	38,163	0	38,163
Rice University, Houston	34,028	0	34,028
Rensselear Polytechnic Inst., Troy	23,163	0	23,163
Wesleyan University, Middletown	21,801	0	21,801
Hunter College, City U. of N. Y., N. Y.	17,461	0	17,461
Amherst College, Amherst	24,390	0	24,390
Arizona State University, Tempe	28,062	0	28,062
Case Western Reserve Univ., Cleveland	45,304	0	45,304
University of Kentucky, Lexington	19,766	0	19,766
Temple University, Philadelphia	30,562	0	30,562
Southern Illinois University, Carbondale	18,670	0	18,670
St. University of New York at Albany	37,569	0	37,569
Catholic University of America, D. C.	20,279	0	20,279
Yeshiva University, N. Y.	19,609	0	19,609
U. of Vermont St. Agri. Col., Burlington	25,744	0	25,744
City U. of N. Y. Grad. Sch. and U. Ctr.	20,908	0	20,908
Colorado State University, Ft. Collins	30,496	0	30,496
Drexel University, Philadelphia	17,943	0	17,943
Oakland University	23,561	0	23,561
City College of the City University of N. Y.	17,490	0	17,490
University of Texas, Dallas	28,291	0	28,291
University of Montana, Missoula	19,262	0	19,262
University of California, Santa Cruz	21,330	0	21,330
Georgetown University	18,623	0	18,623
University of Denver, Colorado	31,117	0	31,117
Haverford College	24,146	0	24,146
Northeastern University, Boston	18,952	0	18,952
Western Michigan University	17,794	0	17,794
University of Houston	19,276	0	19,276
Totals as of April 5, 1974	4,533,000	0	4,533,000

*No fiscal year 1974 awards have been made as of April 5, 1974, the time this information was prepared. Awards totaling $6,007,000 are to be made during the month of April.

Grand Total, General Research Support Grant and Biomedical Sciences Support Grant Awards..............	33,576,000	33,486,217	67,062,217

IMPOUNDED FUNDS RESTORED

Mr. Flood. Also for the record—take a look at page 181 of your justifications—we want a revision of that table to reflect the awarding of the restored 1973 funds in fiscal year 1974, and show the impact of that action on fiscal 1975.

Dr. Bowery. We have that information available.

[The information follows:]

Obligations by Budget Mechanism
Showing "True" Program Levels
in 1974 - 1975

(Amounts in thousands)

Budget Mechanism	1972 No.	1972 Amount	1973 No.	1973 Amount	1974 No.	1974 Amount	1975 No.	1975 Amount
Grants								
Special								
General Research Support	498	$55,212	495	$26,124	490	$86,826	67	$7,270
General Clinical Research Centers	83	42,181	83	41,300	83	42,531	83	42,485
Biotechnology Resources	52	10,924	53	10,500	55	11,693	46	11,715
Animal Resources	87	17,337	86	16,547	98	17,863	83	16,934
Total Grants	720	125,654	717	94,471	726	158,913	279	78,404
Fellowships								
Non-competing	6	66	1	5	6	57	16	217
Competing	1	12	1	6	--	--	--	--
New	5	47	2	21	17	234	3	42
Supplemental	--	--	--	--	--	--	--	--
Subtotal	12	125	4	32	23	291	19	259
Training Grants								
Non-competing	5	183	5	178	6	369	4	75
Competing	3	150	2	82	--	--	--	--
New	--	--	--	--	--	--	--	--
Supplemental	(2)	19	(2)	15	(1)	68	--	--
Subtotal	8	352	7	275	6	437	4	75
Research and Development Contracts	17	2,114	16	2,002	18	1,580	17	1,430
Research Management and Program Services	--	1,948	--	2,184	--	2,486	--	2,532
Total	757	130,193	744	98,964	773	163,707	319	82,700

Obligations by Budget Activity
Showing "True" Program Levels
in 1974 - 1975
(Amounts in thousands)

Budget Program	1973		1974		1975	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Special Programs						
Clinical Research	--	$41,300	--	$42,531	--	$42,485
Biotechnology Research	--	10,704	--	11,923	--	11,945
Laboratory Animal Sciences and Primate Research	--	17,647	--	18,941	--	17,468
General Research Support	--	21,124	--	78,826	--	0
Minority Biomedical Support	--	5,000	--	8,000	--	7,270
Chemical Biological Information Handling Research	--	1,005	--	1,000	--	1,000
Research Management and Program Services	77	2,184	72	2,486	72	2,532
Total	77	98,964	72	163,707	72	82,700

Distribution of 1973 Impounded Funds
(Amounts in thousands)

Budget Mechanism	No. of awards	Amount	Remarks
Special Programs			
General Clinical Research Centers	1	$807	Clinical Research
Biotechnology Resources	1	364	Biotechnology Research
Animal Resources	5	790	Laboratory Animal Sciences and Primate Research
General Research Support	8	34,576	General Research Support $33,576,000, 439 supplementals; Minority Biomedical Support $1,000,000, 8 new awards
Fellowships	7	94	Laboratory Animal Sciences and Primate Research
Training	--	141	Laboratory Animal Sciences and Primate Research (Funds used to increase current year awards)
Total	22	36,772	

GENERAL RESEARCH SUPPORT GRANTS

Mr. FLOOD. Take a look at page 181 of your justifications. There you show 67 grants and $7.2 million for general research support. I thought you said in your opening statement that you are requesting no funds for general research support grants. If that is the case, what is this $7.2 million doing in the 1975 column?

Dr. BOWERY. Within the general research support program there are basically two major program elements. One is the formula award element, the general research support grants and biomedical sciences support grants, that are made to some 400 institutions. The other is the minority biomedical support program awards that are made to minority institutions. The figures on page 181 refer to the anticipated payment of 67 grants for $7.2 million to these minority institutions.

Mr. FLOOD. Can you elaborate on the decision to eliminate the general research support grant program in fiscal 1975? We want the rationale behind this decision. If you can't do this right now, do it for the record. You can imagine why.

Dr. BOWERY. I think the clearest way to state the rationale is, with your permission, to quote from a letter the Secretary sent to a Member of Congress back in January of this year.

Mr. FLOOD. The Secretary?

Dr. BOWERY. The Secretary of DHEW.

Mr. FLOOD. He sent the letter?

Dr. BOWERY. Yes, sir.

Mr. FLOOD. Go ahead.

Dr. BOWERY. Quoting from the letter written to a Member of Congress:

> As you know, the Department is now preparing its budget for fiscal year 1975. During this process, each of our programs is very carefully examined and decisions on program priorities and funding levels are made in light of the need to fulfill valid Federal roles, and to achieve sound purposes. This approach is especially urgent in view of the need to contain Federal expenditures at a level to avoid tax increases and excessive inflation.
>
> In our view, the general research support grant program, which is designed to provide untargeted research funds to institutions to strengthen their biomedical research capacity, is of a lower priority than are program oriented research project activities. In the overall National Institutes of Health budget, we place a relatively higher priority on maintaining financial and programmatic flexibility within the research project grant component of the National Institutes of Health.

Based on that rationale, and concurrent with the release of the President's budget for fiscal 1975, the decision was made to transmit the budget to the Congress requesting no funds for the general research support grants and the biomedical sciences support grants.

Mr. FLOOD. In other words, you can take a hint?

Dr. BOWERY. It was more than a hint, sir, it was a statement.

Mr. FLOOD. I withdraw the word "hint." I was understating.

Anyhow it came from the top down. You didn't give birth to it?

Dr. BOWERY. That is correct.

Mr. FLOOD. In that communication, which I have heard about, can you explain what is meant by the term "untargeted research"? You used that in your opening statement. Give me the answer to that. That doesn't sound like you. What is that?

Dr. BOWERY. When the general research support funds are made available to an institution the decision as to where and how they expend those funds for biomedical research purposes resides within the institution. They have broad authority in making the decision as to how they should be utilized. Therefore, although all of those funds are used for biomedical research in such areas as heart disease, cancer, arthritis, et cetera, they are not targeted inasmuch as the target was not selected by the NIH nor the Department.

Mr. FLOOD. That makes sense.

In this missile you got from the Secretary—in the Department of Defense appropriations we talk about MIRV. That missile you got from the Secretary uses the phrase "financial and programmatic flexibility." That is a beauty. Even for OMB that is quite a phrase. What do you think "financial and programmatic flexibility" means?

Dr. BOWERY. I think there are three basic factors involved in our decision regarding this program.

First, the need for greater fiscal constraints forcing a more rigorous establishment of priorities.

Mr. FLOOD. You sound as bad as he does.

Dr. BOWERY. These are some of my own words.

Mr. FLOOD. No. You have been infected. Better get an antibiotic for that.

Dr. BOWERY. I will look to my categorical colleagues for that.

Mr. FLOOD. In words of not more than eight syllables tell us about it.

Dr. BOWERY. Second, the need to determine within these priorities where we wanted flexibility of choice—within the specific categorical project components of the NIH—historically the hallmark of the NIH extramural effort—versus that of general institutional support.

Third, realizing that even though flexible support and local decisionmaking at the institutional level were valid concepts, the NIH priorities called for a change in the allocation process from general to specific.

PRIMARY REASON FOR GRS PHASEOUT

Mr. MILLER. I want to state, Mr. Chairman, I think that letter and I think the discussion so far has been reason No. 2, not reason No. 1. I think the business of reordering priorities and fiscal constraints is valid, but certainly it is not enough of a reason. I think reason No. 1 is one that Dr. Stone gave in his testimony, which is that the original purpose of that program was to help out the departments of science when we were flooding them with project grants and they needed free money of their own in order to build a broader base over which they would have discretion. We have done that. I think the Federal Government has substantially secured those departments of science. We can pullout now and they can handle it on their own.

This money, which is allocated on a formula basis, goes to the richest grantees—because the more research grant money they receive, the more general research support grant money they get. I don't think the system is equitable. We don't need to put that kind of money into the Harvards and the universities of California.

Mr. FLOOD. Is all of that general research support money going to be used for untargeted research?

Dr. Bowery. I myself personally do not know to what areas that money was allocated.

Mr. Flood. Aren't you curious?

Dr. Bowery. I am curious, yes.

EXAMPLES OF GRS USE

Mr. Flood. If we completely eliminate this program we also eliminate a source of support for the researcher with innovative, unorthodox ideas. He is a dead pigeon, isn't he? He will never get off the ground.

Dr. Bowery. There still is available an opportunity for individuals to file applications with innovative, unorthodox ideas with the categorical institutes and seek support through those nationally competitive programs.

Mr. Flood. Yes; the Postal Service is still operating.

Now you have said that and now the applications are accepted. Suppose you give me an idea of the kind of untargeted research the GRS programs have supported in the last couple of years which have contributed to the overall research goals of NIH.

Dr. Bowery. It is difficult to identify specific instances because the GRS funds have supported over 7,000 research projects which cover some 100 diverse scientific disciplines in the biomedical sciences. These range over wide fields, such as neurological diseases, endocrinological and cardiovascular problems; the infectious and parasitic conditions, metabolic disorders, et cetera. There is a vast array of activities where both younger projects and more mature projects have been supported. I will supply for the record some specific instances of these.

Dr. Stone. Are you specifically interested in unorthodox and unconventional research support in that way?

Mr. Flood. Yes, and then also what you consider more orthodox. Two or three of each.

[The information follows:]

Examples of Unorthodox and Orthodox Biomedical Research Supported by General Research Support Grants

UNORTHODOX

General research support enabled a team of investigators to conduct pilot work on the development of a device that transmits visual information to the brain via the sense of touch. With it, blind subjects in the laboratory have comprehended visual images as though they had sight. Images observed by a television camera are transmitted to Teflon-tipped points which vibrate against the skin on the back of the subject in patterns that duplicate the image of objects scanned by the camera. Pressure sensitive nerves in the skin of the back transmit the images to the brain.

Initial success in this unorthodox research led to categorical project grant funding from the NIH for further research to seek a practical substitute for vision that could be employed by the blind.

Scientists have used a general research support grant at Purdue University to determine whether certain alkaloids would inhibit the growth of tumors in milk-producing glands. These alkaloids were known to prevent milk formation in man and animals, but they had not been found to be effective against cancer.

As a result of their investigations, these doctors found that the alkaloids inhibited mammary tumors in rats, and they discovered that one of the compounds caused complete disappearance of the tumors. However, the dose needed approached a toxic level, and the compound was considered unsafe. This led to the synthesis of new compounds related to the original alkaloids that will be tested for safety and effectiveness against the rat mammary tumors.

A graphic test to detect abnormal development in infants and small children was developed under a general research support grant. Called the Denver Developmental Screening Test (DDST) it is simple to administer, easy to score, and can be used for repeated evaluations of the same child.

Under the test format, an individual child's performance can be compared quickly with other children on a standardized scale for four major functional areas: gross motor, fine motor-adaptive, language, and personal-social. The DDST is not an intelligence test, but is a screening device to detect children with developmental delays. When delays in development are detected during infancy and the preschool years, it significantly increases the opportunities for effective therapy.

The new screening test has been recommended to the Nation's pediatricians by the Americal Academy of Pediatrics and was used in Project Head Start.

ORTHODOX

At Pennsylvania State University, College of Medicine, scientists observed that certain inbred guinea pigs in a colony had developed diabetic-like changes of the pancreas, the insulin-producing gland. With a general research support grant, they found that these changes were accompanied by high levels of sugar and cholesterol in the animal's blood and urine, and that the ones affected occurred according to genetic principles. This is an animal model that can be used to investigate various aspects of diabetes mellitus.

General research support was used at a hospital to provide computer facilities needed for a wide variety of biomedical research. The studies serviced by the computer include pulmonary and cardiac physiology investigations; determination of optimal dosages for radiation therapy; developing solutions to complex research equations; and the storage and retrieval of extensive psychiatric research information.

The Palo Alto Medical Research Foundation used general research support to initiate a bioengineering project to gain new knowledge on the functioning of the urinary bladder. An optical device was developed for direct observation of the urinary outflow tract without significant interference with bladder function. Incorporated in this new instrument were fiber optics (light pipes) for illumination, and sensing devices to measure continuously urine flow and pressure while observing action of the sphincter that controls the voiding of urine.

GRADUAL PHASEOUT OF GRS GRANTS

Mr. Flood. If this general research suport program is such a low priority and you think it is better to place a higher priority in the 1975 budget on research projects which are grant components of NIH, wouldn't it make better sense to phase out this kind of program gradually and thus give the institutions time to obtain other sources of support instead of bang, cutting it off?

Dr. Bowery. If you look back in the budgetary requests submitted to Congress during the appropriation process in fiscal years 1973 and 1974 the request had been made to reduce the program from around $50 million down to $20 million and eventually down to $9.5 million. Congress, however, through its appropriation process restored the funds to higher levels. Therefore, an attempt was made to request a slow phaseout of the program.

Mr. Flood. There was an attempt made?

Dr. Bowery. Appropriation requests were put before this committee indicating a gradual reduction of approximately 50 percent per year for over a 3-year period.

Mr. Flood. What about now? What about next year's? It is cut out altogether, apparently. Wouldn't a phaseout be better even now or anytime, and give them a chance to look around and get support someplace else?

Dr. Bowery. It would allow for an easier transition by the institutions.

Mr. Flood. Sure it would. But you are not going to do that.

Dr. Bowery. The request before you does not do that.

Mr. Miller. I think the only justification, Mr. Chairman, is that we put them on notice 2 years ago. We said "We want to phase this program out so you better get ready to find other means of support." We felt that was enough notification. However, I do think that phase down rather than out is not inequitable.

EFFECT OF GRS CUT ON INSTITUTIONS

Mr. Flood. We have heard testimony here in the last week—I think you were here for a while—concerning the need to do more cancer research, heart research, and so on. After all of that testimony we have been hearing all week, don't we need strong research institutions to carry out that research? How are you going to do all of these grand things you want done in research if you don't have the institutions to carry out the research? That seems to follow like night follows day. Doesn't the elimination of general research support grants weaken the very institutions that we are counting on to conquer heart disease and cancer as well as make inroads into any other major diseases? Are you destroying your weapons?

Dr. Bowery. I don't think it weakens the institution. It may reduce the flexibility for some of the key members in the leadership roles in these institutions. But over the past 10 years of this program awarding at, say, an average of $50 million per year the capacity has been built. I don't think that capacity is being destroyed by the termination of this program.

CLINICAL RESEARCH CENTERS

Mr. Flood. Last year you told the committee that in the clinical research centers some of the basic hospital care and the treatment costs would be covered by a third party, an insurance company. Here is a request of $42.4 million for the clinical research centers. Have you taken into consideration the amount to be collected from the insurance companies, and have you only requested the balance?

Dr. Bowery. That is correct.

Mr. Flood. Will you provide for the record how much each center collected from insurance companies in fiscal years 1972 and 1973 and give us an estimate for 1974 and 1975.

[The information follows:]

Policy for Third party payments - Clinical Research Program

On October 1, 1968, Program policy was modified to allow grantees the option of admitting "service patients" to the Clinical Research Center. The service patient is defined as "a patient admitted to a CRC primarily for care," although he may also be participating in a research protocol. The service patient is fiscally responsible for the expenses of providing his care in the CRC, just as he would if he were admitted to a regular hospital bed. As defined below, service patients are further classified between those participating in a research protocol (category B) and strictly non-research patients (category C).

The three categories of patients who may be admitted to the GCRC are defined as follows:

Category A. Research Patients

Those patients admitted to the CRC primarily to participate in a research protocol.

Category B. Research Service Patients

Those patients admitted to the CRC primarily for the purposes of diagnosis or treatment according to established therapeutic regimens, and who are participating in a CRC research protocol that may or may not be related to their illness.

Category C. Non-research Patients

Those patients admitted to the CRC solely for the purposes of diagnosis or treatment according to established therapeutic regimens and who are not participating in a research protocol.

The CRC grant pays all costs of Category A patient admissions. Category B patients are fiscally responsible for the costs of their hospitalization. Category C. patients are also fiscally responsible for their hospitalization costs and may be admitted to the CRC only under certain circumstances.

General Clinical Research Centers

Credits for Category B and C Patients

	FY 1972	FY 1973
Duke University	$ 82,638	$ 93,509
Harvard University	80,463	87,525
University of Alabama	27,186	148,816
Ohio State University	1,357	7,294
Johns Hopkins Univ.	155,589	148,596
Washington University	123,605	147,084
University of Washington	-0-	-0-
Emory University	-0-	-0-
University of Pennsylvania	-0-	300
University of Michigan	181,625	107,056
University of Southern California	83,520	106,720
University of Rochester	10,169	27,217
University of North Carolina	41,117	13,133
Cornell University	147,142	131,281
Northwestern University	158,666	207,054
University of Arkansas	117,530	32,541
Albert Einstein	108,062	155,577
University of Colorado	-0-	-0-
Johns Hopkins University	-0-	-0-
Montefiore Hospital	1,800	7,560
New England Medical Center Hospital	107,955	106,689
University of Chicago	-0-	-0-
University of Pittsburgh	-0-	10,268
Medical College of Wisconsin	24,625	19,752
University of Iowa	-0-	-0-
Georgetown University	22,203	42,742
University of Oklahoma	-0-	-0-
University of Puerto Rico	-0-	-0-
University of Utah	136,544	152,090
Virginia Commonwealth University	8,637	68,056
University of Kansas	62,553 1/	
University of Cincinnati	-0-	-0-
University of Colorado	-0-	-0-
Stanford University	148,070	175,913
Mt. Sinai	-0-	-0-
University of Texas	-0-	-0-
Wayne State University	5,705	8,760
St. Christopher's Hospital	-0-	-0-
Harvard	124,394	120,304
Children's Hospital, Columbus	-0- 1/	
University of California, San Francisco	48,147	48,507
University Hospital of Cleveland	46,450	49,351
Stanford University	21,975	-0-
University of Florida	-0-	-0-
University of California San Francisco	-0-	-0-
Children's Hospital, Pittsburgh	-0-	75,333
Children's Hospital, Los Angeles	2,645	27,655
M.I.T.	-0-	-0-
Vanderbilt University	-0-	-0-
New York University, Bellevue	200,250	273,887

1/ Support Phased Out

	FY 1972	FY 1973
Rockefeller University	-0-	-0-
Philadelphia General Hospital	9,444	2,162
University of Vermont	-0-	-0-
Children's Hospital, Cincinnati	-0-	-0-
Yale University	-0-	-0-
Children's Hospital Medical Center	100,485	117,607
University of Washington	8,814	15,595
Baylor University	4,349	10,830
Baylor University	40,312	35,274
Children's Memorial Hospital, Chicago	12,000	22,948
Case-Western Reserve	21,123	45,626
University of Tennessee	4,420	19,379
St. University of New York, Syracuse	-0-	-0-
Children's Hospital of Philadelphia	20,380	39,115
University of Miami	-0-	-0-
Roswell Park	-0-	-0-
Children's Hospital, D. C.	93,950	114,794
University of Missouri	-0-	-0-
University of Virginia	-0- 1/	
University of Chicago	3,235	1,380
St. University of New York, Downstate	1,900	36,600
University of Pennsylvania	111,499	-0-
University of Oregon	-0-	-0-
Bowman Gray	5,104	900
Temple University	22,338	60,255
Baylor University	78,890	117,114
University of Minnesota	28,321	2,100
Harbor General Hospital	-0-	-0-
Boston University	-0-	-0-
Mayo Foundation	-0-	-0-
University of Mississippi	5,426	1,400
Children's Hospital of Buffalo	24,000	25,350
University of Texas	Not Open	Not Open
Columbia University	Not Open	29,567
University of Arizona	18,439	18,811
Johns Hopkins (Outpatient)		Not Open
Albany Medical College	28,163	32,197
Indiana University	12,068	5,411
Total	$2,935,282	$3,354,985

1/ Support Phased Out

It is estimated that third parties collections will be approximately $3,589,834 in FY 1974 and $3,948,817 in FY 1975. The availability of third party payments for research patients varies widely depending on the type of studies at each center and the condition of the patients under study. NIH policy does not permit consideration of the availability of third party payments to be a criterion for admission to a research study.

Mr. FLOOD. How many beds did you support in fiscal 1974?

Dr. BOWERY. In the neighborhood of 882 to 890 beds.

Mr. FLOOD. How many will you support in fiscal 1975?

Dr. BOWERY. We are projecting a support of 840 beds.

Mr. FLOOD. Last year you told this committee that the average daily census was 622 beds in 1970, 588 in 1971. If the average daily census is declining like that, as it has, to 600, why are you requesting support for approximately 840 beds in 1975? Why not cut the request down to the support of 600 beds?

Dr. STONE. Mr. Chairman, that is to some extent a peculiarity of the operation of hospitals, and it is more true of research beds than of general hospital beds.

A good hospital administrator attempts to run at an occupancy rate of about 85 percent. The extraordinary needs of a clinical research program require an occupancy rate somewhat lower for really optimum operation of the units. There is always some slack in the use of the beds there, but there is no slack in the use of the total resources that are available. That is, the nurses, the dieticians, the physicians, and the laboratories are used full time.

Mr. FLOOD. Do you pay the same rate to the hospital whether the bed is occupied or not?

Dr. STONE. I will ask Dr. Bowery.

Dr. BOWERY. We tend to "rent" space from the hospital for the physical area where the general clinical research center is located, which includes the beds. Costs for ancillary services are only paid on the basis of actual utilization.

Mr. FLOOD. For the record, give us the occupancy rate for each of these clinical centers in 1971, 1972, 1973, 1974.

Dr. BOWERY. Yes, I will do that.

Mr. FLOOD. In the case of fiscal 1974 just give it to us for the first 6 months and also, if you can, an overall occupancy rate for each fiscal year. You might have a problem with that.

Dr. STONE. Might we include some comments on the question of occupancy rates for research beds? I think it would be clarifying.

Mr. FLOOD. All right.

[The information follows:]

HOSPITAL BED OCCUPANCY RATES

Hospital bed occupancy rates are calculated on the basis of patient days divided by available bed days (bed spaces times 365 days per year). Acute general care and research hospitals strive to attain the highest rate of bed occupancy possible. Since, in general, the costs of maintaining an empty bed are nearly equal to those associated with one which is occupied, it is essential that the hospital bed occupancy rate be maintained at the optimal level if the resources (that is, space, staff and funds) are to be effectively utilized.

The most effectively managed acute general care hospitals rarely achieve an occupancy rate greater than 85 percent. Full occupancy is never achievable since a portion of available time is lost through the scheduling of departures and new admissions, the unavailability of patient care staff, the availability of specialty beds (for example, the number of beds allocated for obstetrics which cannot be used for other purposes), et cetera. These problems are further compounded in the research setting where the occupancy rate tends to run nearer 70 percent. The units which reflect an ocupancy rate greater than 100 percent are normally units which have a greater number of beds than is being supported by the grant or has added outpatient areas which are not counted in the bed complement. In units with an overflow capacity, category B or C class patients may be admitted to these units. No charge is made to the grant, however, a credit is given to the grant for those services which are supported directly by the grant (that is, nursing, dietary and space). The great majority of patients, or subjects, admitted to research centers are elective admissions at the patient's convenience. Therefore, occupancy tends to be quite low on weekends and during holiday periods, particularly in children's units. Furthermore, most research units are relatively small and have some difficulties in scheduling the mix of patients by age, sex, and types of research problems into available facilities.

In the general clinical research centers program, centers are permitted to utilize outpatients, where appropriate, in the conduct of the research, in addition to inpatients. A substantial number of the centers supported by this program do, in fact, utilize outpatients, and in fiscal year 1973 they recorded approximately 35,000 outpatient visits. For the purpose of this analysis, outpatients, who are attended by research personnel and who utilize research funds for ancillary services such as X-ray and laboratory tests, et cetera, have been included at the ratio of three outpatient visits to one inpatient day.

The costs of operating the program vary relatively little with actual patient occupancy. In 1970, the program changed accounting systems such that space is in essence "rented" from the hospital while ancillary services are purchased on an item-by-item basis. Personnel who provide 24-hour coverage 7 days a week are directly funded by the grant. Thus, in fiscal year 1974, 1,767 full-time positions, including doctors, nurses, technicians, dieticians, and secretaries, were funded at a cost of $22,432,000 plus indirect costs. Space charges, including indirect costs, administrative costs, maintenance, laundry, food, and the like, are individually negotiated on a center-by-center basis. In fiscal year 1974, the program supported roughly 530,000 square feet. A typical center contains approximately 6,000 square feet including 10 beds, a nursing station, a conference room, outpatient offices, a diet kitchen, a core laboratory, a lounge (play area), and treatment room (procedures). Ancillary purchases vary from center-to-center but are expected to average about $55 per patient day in fiscal year 1974. Thus, it can be seen that the major costs of funding a research unit are fixed in personnel and space charges.

Clinical Research Centers
Beds & Occupancy

	FY 1971		FY 1972		FY 1973		FY 1974
	No. of Beds	% of Occ.	No. of Beds	% of Occ.	No. of Beds	% of Occ.	No. of Beds 3/
Duke University	17	84.2	17	88.8	17	81.1	17
Harvard University	18	96.5	24	76.7	16	96.2	16
University of Alabama	10	73.8	10	78.9	10	82.3	10
Ohio State University	10	50.8	10	63.0	10	70.7	10
Johns Hopkins University	16	92.6	21	67.3	21	67.8	21
Washington University	33	84.2	33	79.1	33	72.6	33
University of Washington	16	62.5	16	68.2	16	85.9	16
Emory University	10	89.0	10	102.8	10	100.9	10
University of Pennsylvania	10	63.3	10	61.1	10	60.2	10
University of Michigan	20	85.1	20	81.8	20	75.7	15
University of Southern Calif.	10	91.9	10	90.1	10	81.3	10
University of Rochester	8	89.1	8	87.6	8	94.6	8
University of North Carolina	12	60.6	12	72.3	12	62.9	12
Cornell University	24	71.6	24	69.3	24	79.3	12
Northwestern University	9	90.5	8	99.4	8	102.4	8
University of Arkansas	8	108.5	8	138.9	8	143.1	4 1/
Albert Einstein	12	49.2	12	39.6	12	54.9	12
University of Colorado	18	83.8	18	91.3	18	99.3	18
Johns Hopkins University	12	53.3	12	61.4	10	52.6	8
Montefiore Hospital	15	76.5	16	64.0	16	60.6	16
New England Medical Center Hosp.	14	55.3	14	71.8	14	58.5	14
University of Chicago	10	86.8	10	86.8	12	59.1	10
University of Pittsburgh	14	48.2	14	34.5	10	43.1	10
Medical College of Wisconsin	12	70.2	10	77.6	10	70.0	10
University of Iowa	10	122.4	14	105.6	12	113.7	12
Georgetown University	12	68.2	16	62.6	16	75.6	10
University of Oklahoma	10	75.3	10	56.2	10	71.4	10
University of Puerto Rico	12	62.4	12	66.2	12	55.9	12
University of Utah	15	51.2	15	70.9	15	68.2	15
Virginia Commonwealth Univ.	10	54.5	10	57.4	10	68.6	10 1/
University of Kansas	8	79.7	6	106.4 1/			

	FY 1971		FY 1972		FY 1973		FY 1974
	No. of Beds	% of Occ.	No. of Beds	% of Occ.	No. of Beds	% of Occ.	No. of Beds 3/
University of Cincinnati	6	106.6	6	132.8	6	92.2	6
University of Colorado	6	84.7	6	88.6	6	85.0	6
Stanford University	16	76.3	16	76.4	16	65.7	16
Mt. Sinai	9	81.2	9	70.2	9	76.2	9
University of Texas	12	75.5	12	76.7	12	66.6	10
Wayne State University	6	54.1	6	60.7	3	69.8 1/	
St. Christopher's Hospital	8	69.0	8	68.3	8	66.5	8
Harvard University	18	67.4	18	59.1	18	66.2	14
Children's Hospital - Columbus	6	95.9	6	91.5 1/			
Univ. of California, S.F.	18	69.6	18	72.5	18	60.7	18
University Hosp. of Cleveland	10	71.5	10	75.9	8	90.8	8
Stanford University	6	85.1	6	76.3	6	59.1	6
University of Florida	10	56.4	8	72.4	8	64.0	7
Univ. of California, S.F.	9	55.6	9	50.1	9	57.3	9
Children's Hospital, Pittsburgh	6	65.3	6	68.9	5	57.8	6
Children's Hospital, L.A.	6	67.5	6	73.4	6	72.5	6
Mass. Institute of Technology	10	106.5	10	122.7	12	85.4	10
Vanderbilt University	21	61.9	21	66.5	21	91.1	21
N.Y.U., Bellevue	13	97.5	13	73.3	13	85.9	13
Rockefeller University	30	71.5	30	88.9	30	77.1	30
Philadelphia General Hospital	5	86.5	8	55.3	4	71.9	8 1/
University of Vermont	6	60.6	6	86.2	6	77.5	6
Children's Hospital, Cinn.	8	62.8	8	57.6	8	60.5	8
Yale University	16	55.0	16	69.2	16	59.0	15
Children's Hosp. Med. Ctr., Boston	10	58.3	10	60.2	10	61.2	10
University of Washington	6	79.3	6	68.2	6	70.6	6
Baylor University	6	90.0	6	84.2	6	83.7	6
Baylor University	8	56.4	8	47.8	6	70.5	6
Children's Mem. Hosp., Chicago	6	88.5	6	72.5	6	76.4	6
Case Western Reserve	8	78.0	8	88.6	8	73.5	8
University of Tennessee	10	71.3	10	68.8	6	69.8	6
St. Univ. of N.Y., Syracuse	10	79.0	10	64.0	10	64.1	10
Children's Hosp. of Phila.	4	75.3	4	85.3	4	80.7	8
University of Miami	14	69.2	14	68.5	14	65.7	14

	FY 1971		FY 1972		FY 1973		FY 1974
	No. of Beds	% of Occ.	No. of Beds	% of Occ.	No. of Beds	% of Occ.	No. of Beds 3/
Roswell Park	10	118.4	10	116.8	10	136.0	10
Children's Hospital, D.C.	8	48.3	8	46.8	5	57.9	5
University of Missouri	6	78.3	6	88.5	6	80.7	9
University of Virginia	10	64.2	5	91.6	5	79.6 1/	
University of Chicago	5	82.6	5	58.8	6	65.4	6
St. U. of N.Y., Downstate	10	57.0	10	63.4	8	74.3	8
University of Pennsylvania	5	90.7	5	46.6	5	50.0	5 1/
University of Oregon	4	66.7	4	71.7	4	91.8	4
Bowman Gray	6	57.3	6	64.1	6	83.7	4
Temple University	5	145.3	5	104.2	8	75.9	8
Baylor University	12	108.8	14	68.8	14	65.6	14
University of Minnesota	11	56.6	11	69.6	11	56.3	10
Harbor General Hospital	8	66.0	8	81.1	8	89.0	8
Boston University	8	60.6	8	63.2	8	57.9	8
Mayo Foundation	13	77.7	13	77.7	12	57.1	13
University of Mississippi					5	96.7	5
Children's Hospital of Buffalo	6	40.6	6	48.2	6	56.2	5
University of Texas							13
Columbia University					4	61.3	4
Arizona University					2	85.8	2
Albany Medical Center					8	56.2	8
Indiana University					4	60.2	8
Univ. of California, L.A.							8
University of Virginia							7
Scripps							6
University of Kansas							5
Univ. of California, San Diego							8
Total Beds Funded	885		898		879		890
Total Patient Days		240,173 2/		240,490 2/		237,661 2/	236,094 (est.)
Total Occupancy		74.4%		73.4%		74.1%	72.7%(est.)

1/Terminal Year

2/Total includes patient days paid by third parties and outpatients (3 outpatient visits = 1 patient day)

3/Data insufficient for FY 1974 to show occupancy comparability on a center-by-center basis. Overall occupancy rate estimated.

ANIMAL RESOURCES

Mr. **Flood.** On the animal resources, in your opening statement you said the importation of primates is limited and this is going to become a serious problem. Yet on page 188 of your justifications you show an overall reduction of $500,000 in the laboratory animal sciences and the primate research program. How do you plan to meet the research need for more primates with less money? How do you do that? It seems to me from the appropriation point of view it takes Houdini to do that.

Dr. **Bowery.** The approach we are using is to take some of the limited funds and develop some small operational contracts with commercial enterprises to develop the feasibility of breeding primates here in the United States. This will give us an opportunity with this small investment of contract funds to begin to meet about 40 percent of what we estimate to be the NIH extramural research needs for primates. We will particularly focus on the rhesus monkey, the major species on which we are having importation problems with India.

EFFECTS OF MARIHUANA ON SOCIAL BEHAVIOR

Mr. **Flood.** In your justification you mention the study to measure the effects of marihuana on social behavior and the endocrine system. Can you tell us more about that study and your findings to date?

Dr. **Bowery.** Essentially the level of activity reported here is the latest on which we have knowledge. It appears that this effect on the endocrine system may bring some slowly developing basic changes in personality of the animals perceived and in their emotional and reproductive responsivity and the levels of sex hormones as well as stress-response hormones. I think it is much too early to see, and the trial at this stage is too small to draw any conclusive relationship between these observations on the nonhuman primates and the potential impact upon a human subject.

We will watch this closely, and, if the committee so pleases, we can get an update from the California center as to the precise nature of the studies at this time.

Mr. **Flood.** Good.

[The information follows:]

Effects of Marihuana of Social Behavior and Endocrine Systems in Primates

Continuation of daily drugging of rhesus monkeys up to 9 months with tetrahydrocannabinal, the major component of marihuana, at levels comparable to heavy use in humans, has produced marked effects on both social behavior and reproductive function, especially in postpubertal females. After 9 months of drug exposure, the monkeys no longer show evidence of the sedative effects of the drug. On the other hand, the females have become more aggressive, and the social hierarchy has been upset. These observations in monkeys suggest that drug effects on behavior may be most marked in the less secure members of the group. Similar observations have been made in man.

This research is being continued and is directly concerned with answering the question as to whether or not chronic exposure to marihuana leads to long-lasting deleterious residual changes in social and emotional behavior, changes in neuroendocrine systems, and damage to the brain.

PRIMATE CENTERS

Mr. **Flood.** Do any of the other Federal agencies, such as the Department of Defense, pay for the cost of maintaining the primate centers?

Dr. **Bowery.** Not that I am aware of. Some of the primate centers may have some separate individual contracts from the Department of Defense.

Mr. **Flood.** How much of any other Federal money is invested in the primate centers? Do you know?

Dr. **Bowery.** The last estimate that I was aware of was around $7.4 million additional funds coming in from various sources, including some of the categorical institutes of NIH.

Mr. **Flood.** Is there any private money invested in the centers?

Dr. **Bowery.** I would judge that there is some but I don't know the actual amount at this time.

Mr. **Flood.** Tell me how much.

Dr. **Bowery.** We will supply you a breakout of the funds received by the primate centers, including that from the Division's budget, the categorical institutes and other sources.

[The information follows:]

The following is a breakdown of funds received by the primate centers for fiscal year 1973 which is the latest information available at this time.

Type of organization	Number of awards	Amount
Research resources appropriated funds	[1] 8	$11,347,000
NIH categorical institutes	86	5,960,693
Other Government agencies	17	701,474
Nonprofit organizations	31	735,357
Total	142	18,744,524

[1] Includes contract for the Holloman Air Force Base Chimpanzee Breeding Colony.

COMPUTER SYSTEM

Mr. **Flood.** Tell us more about your computer system called "PROPHET." Who are the users?

Dr. **Bowery.** In my opening statement I indicated that we have users at four geographically dispersed installations. As of February of this year we had a group at the department of pharmacology, the School of Medicine, the University of Pittsburgh in Pennsylvania; at the Harvard Medical Unit of the Thorndike Memorial Laboratory in Boston City Hospital, in Boston, Mass.; the department of pharmacology, Mt. Sinai School of Medicine, City of New York University in New York; molecular biomedical department in Buffalo, N.Y.; and recently we have added a fifth group at the Research Institute on Alcoholism, New York State department of mental hygiene at State University of New York at Buffalo. That is our current dispersement.

Mr. **Flood.** Do the individuals that use this pay a charge for the amount of time they use the system? Do you charge in the same way a time sharing computer company would charge for using the system?

Dr. Bowery. Not in this stage of the evolution of the system. We plan to slowly introduce a fee for service charge after the system has evolved further. Basically we are developing this interactive computer tool for the use of scientists in drug research, and we don't want to establish—early on—a cost barrier to them. We wanted to see whether they felt it was feasible; whether it would serve their scientific needs and interest; and whether the system would facilitate scientific communication with other people involved in pharmacology research. Once they have accepted the system scientifically and it is helping them, their willingness to pay a fee for the service would be more easily obtained.

ABOLITION OF THE DIVISION

Mr. Flood. I hear a rumor that the Division of Research Resources might be abolished. Any truth in that rumor? Is that actually being considered?

Dr. Stone. I will respond to that if I might.

Mr. Flood. Yes.

Dr. Stone. We certainly have an option paper that reviews that possibility. It is something that was considered by my predecessor. My understanding is that he was close to making a decision as to whether or not there should be some organizational changes at the time he left the office of the director. We are reexamining it. I don't know what the outcome will be at this time.

Mr. Flood. That has been kicking around for a while.

Dr. Stone. Yes, really quite a long time. It has come up again and again. I think we have to dispose of it in one way or another.

Mr. Flood. Who would carry on the work of the Division of Research Resources if you abolish the program?

Dr. Stone. The work would not be eliminated.

Mr. Flood. Who would do it?

Dr. Stone. The Clinical Research Centers, for example, might be put into the Arthritis, Metabolic, and Digestive Diseases Institute because there are natural affinities between the programs that institute supports and the work done in many of the centers.

The animal resources support system might be associated with the general animal resource support program in NIH.

The program you were just talking about, PROPHET, could be affiliated with the pharmacology-toxicology program in NIGMS. Because it is an information handling system, it might be affiliated with the National Library of Medicine.

There are other possibilities that I think we should look at in terms of organizational efficiency and effectiveness.

MINORITY BIOMEDICAL SUPPORT GRANTS

Mr. Flood. How many minority biomedical support grants did you fund in fiscal 1974?

Mr. Chicchirichi. We expect by the end of the year, Mr. Chairman, to fund a total of 60 during 1974. This includes the continuation of the grants that were awarded beginning in 1972 plus several new ones during 1974.

Dr. Stone. About a week and a half ago, I visited the Atlanta University Center in Atlanta and examined the minority biomedical support program there. I was enormously impressed by the amount of influence that it has had on the several institutions in that center not only in providing encouragement, which is intangible, but also in providing equipment and salaries for individuals. There is a whole new research spirit developing and the availability of some biomedical research support has a tremendous effect on the development of people there. This is something we must try to foster. It was extraordinarily encouraging. I was tremendously impressed by it.

Mr. Flood. In 1975 how many minority biomedical support grants do you expect to award?

Mr. Chicchirichi. We expect that to increase to a total of about 67. This will be approximately eight more than in 1974.

Mr. Flood. Can you tell us the number of individuals that will be supported by these grants in fiscal 1975?

Dr. Bowery. That would be difficult to estimate because we are just starting in the review process for fiscal 1975 applications.

Mr. Flood. Do you have an educated guess?

Mr. Chicchirichi. We have an estimate of approximately 1,300 individuals, including faculty and undergraduate and graduate students.

Mr. Flood. Will you give us for the record a list of the institutions receiving these minority biomedical support grants in 1974 and 1975? Be sure and show the period of the grant, the amount of the grant and the number of people supported.

Dr. Bowery. It will be difficult to indicate those for 1975.

Mr. Flood. Sure it will. That is your problem.

Dr. Bowery. Do you want us to predict?

Mr. Flood. Yes, sure. You predict everything else, you may as well predict that.

[The information follows:]

MINORITY BIOMEDICAL SUPPORT GRANTS

Institution (by State)	1974 Awards Amount	Budget Period	Estimated Faculty/Staff	Estimated Student Participants[3]	1975 Estimated Awards Amount	Budget Period	Faculty/Staff	Student Participants[3]
Alabama								
Alabama State University	$ 52,927	1/1/74-12/31/74	4	7	$ 44,094	1/1/75-12/31/75	4	7
Oakwood College	35,417	1/1/74-12/31/74	4	8	36,792	1/1/75-12/31/75	4	8
Stillman College	78,769	1/1/74-12/31/74	4	17	73,241	1/1/75-12/31/75	4	17
Talladega College	126,772	9/1/73-12/31/74	5	11	88,654	1/1/75-12/31/75	5	11
Tuskegee Institute	186,874	1/1/74-12/31/74	21	28	167,258	1/1/75-12/31/75	21	27
California								
California State University	228,675	1/1/74-12/31/74	17	32	229,908	1/1/75-12/31/75	17	34
Delaware								
Delaware State College	71,360	1/1/74-12/31/74	2	10	72,760	1/1/75-12/31/75	2	16
District of Columbia								
Federal City College	108,040	1/1/74-12/31/74	13	12	110,240	1/1/75-12/31/75	13	12
Howard University	340,138	1/1/74-12/31/74	43	54	274,419	1/1/75-12/31/75	43	37
Florida								
Bethune-Cookman College	137,127[1]	5/1/74-4/30/75	5	11	149,738[1]	5/1/75-4/30/76	5	12
Florida A & M University	183,031	1/1/74-12/31/74	18	20	174,747	1/1/75-12/31/75	18	24
Georgia								
Albany State College	72,497	1/1/74-12/31/74	7	6	68,780	1/1/75-12/31/75	7	6
Atlanta University Center	764,401	1/1/74-12/31/74	40	87	547,192	1/1/75-12/31/75	40	75
Fort Valley State College	116,469[2]	3/1/74-8/31/75	4	8			4	8
Paine College	33,801	1/1/74-12/31/74	3	5	13,986	1/1/75-5/31/75	3	5
Hawaii								
University of Hawaii at Hilo	158,064	1/1/74-12/31/74	9	10	108,064	1/1/75-12/31/75	9	8
University of Hawaii, Manoa	100,919[1]	5/1/74-4/30/75	18	15	107,086[1]	5/1/75-4/30/76	21	19
Illinois								
Chicago State University	62,352	1/1/74-12/31/74	9	18	63,954	1/1/75-12/31/75	9	18

MINORITY BIOMEDICAL SUPPORT GRANTS

Institution (by State	1974 Awards				1975 Estimated Awards			
	Amount	Budget Period	Estimated Faculty/Staff	Estimated Student Participants[3]	Amount	Budget Period	Faculty/Staff	Student Participants[3]
Kentucky								
Kentucky State University	$ 74,403[1]	5/1/74-4/30/75	3	7	$ 54,105[1]	5/1/75-4/30/76	3	7
Louisiana								
Dillard University	61,380	1/1/74-12/31/74	6	8	52,580	1/1/75-12/31/75	6	8
Grambling College	89,200	1/1/74-12/31/74	4	30	84,380	1/1/75-12/31/75	4	37
Southern University, Baton Rouge	206,398	1/1/74-12/31/74	10	19	161,758	1/1/75-12/31/75	10	16
Southern University in New Orleans	116,556	1/1/74-12/31/74	8	12	79,045	1/1/75-12/31/75	8	8
Xavier University of Louisiana	117,007	1/1/74-12/31/74	13	36	132,281	1/1/75-12/31/75	13	35
Maryland								
Coppin State College	63,293	1/1/74-12/31/74	7	12	65,052	1/1/75-12/31/75	7	8
Univ. of Maryland, Eastern Shore	67,060[2]	3/1/74-8/31/75	3	8			3	4
Mississippi								
Alcorn A & M College	43,246	1/1/74-12/31/74	4	12	49,810	1/1/75-12/31/75	4	16
Jackson State College	101,653	1/1/74-12/31/74	8	12	101,988	1/1/75-12/31/75	8	12
Rust College	48,640	1/1/74-12/31/74	4	11	47,320	1/1/75-12/31/75	4	12
Tougaloo College	73,010	1/1/74-12/31/74	4	4	48,644	1/1/75-12/31/75	4	4
Missouri								
Lincoln University	91,903	1/1/74-12/31/74	7	28	89,215	1/1/75-12/31/75	7	30
New Mexico								
New Mexico Highlands University	145,336	1/1/74-12/31/74	19	32	144,905	1/1/75-12/31/75	19	32
University of Albuquerque	85,183	1/1/74-12/31/74	5	14	73,412	1/1/75-12/31/75	5	14
North Carolina								
Bennett College	29,700	1/1/74-12/31/74	2	6	29,000	1/1/75-12/31/75	2	6
Elizabeth City State University	100,718[2]	3/1/74-8/31/75	6	7			6	9
Johnson C. Smith University	48,225	1/1/74-12/31/74	4	10	47,000	1/1/75-12/31/75	4	10
North Carolina A & T State Univ.	164,153	1/1/74-12/31/74	13	18	125,403	1/1/75-12/31/75	13	18
North Carolina Central Univ.	90,957	1/1/74-12/31/74	7	28	91,742	1/1/75-12/31/75	7	32
Shaw University	94,551	1/1/74-12/31/74	8	8	68,968	1/1/75-12/31/75	8	8
Winston-Salem State University	63,301	1/1/74-12/31/74	5	4	38,830	1/1/75-12/31/75	5	6

MINORITY BIOMEDICAL SUPPORT GRANTS

Institution (by State)	1974 Awards Amount	1974 Awards Budget Period	1974 Awards Estimated Faculty/Staff	1974 Awards Estimated Student Participants[3/]	1975 Estimated Awards Amount	1975 Estimated Awards Budget Period	1975 Estimated Awards Faculty/Staff	1975 Estimated Awards Student Participants[3/]
North Dakota								
Turtle Mountain C & R Center	$ 46,980[1/]	5/1/74-4/30/75	3	3	$ 50,623[1/]	5/1/75-4/30/76	3	3
Ohio								
Central State University	44,709	1/1/74-12/31/74	7	6	41,543	1/1/75-12/31/75	7	4
Oklahoma								
Langston University	118,812[2/]	3/1/74-8/31/75	5	8			5	8
Northeastern State College	97,349[1/]	5/1/74-4/30/75	6	10	74,562[1/]	5/1/75-4/30/76	6	12
Southeastern State College	128,087	1/1/74-12/31/74	10	18	109,825	1/1/75-12/31/75	10	18
Pennsylvania								
Lincoln University	109,491	1/1/74-12/31/74	4	14	65,471	1/1/75-12/31/75	3	10
Puerto Rico								
Catholic Univ. of Puerto Rico	99,201	1/1/74-12/31/74	9	10	100,942	1/1/75-12/31/75	9	10
Univ. of Puerto Rico, Mayaguez	145,673[2/]	3/1/74-8/31/75	8	13			8	14
Univ. of Puerto Rico, Rio Piedras	114,470	1/1/74-12/31/74	15	22	110,361	1/1/75-12/31/75	15	24
South Carolina								
Benedict College	155,108[1/]	5/1/74-4/30/75	8	17	119,448[1/]	5/1/75-4/30/76	8	17
South Carolina State College	63,468	1/1/74-12/31/74	5	8	63,796	1/1/75-12/31/75	5	8
Tennessee								
Fisk University	75,768	1/1/74-12/31/74	8	12	87,280	1/1/75-12/31/75	8	12
Knoxville College	59,433	1/1/74-12/31/74	2	8	45,018	1/1/75-12/31/75	2	8
Meharry Medical College	158,247	1/1/74-12/31/74	8	20	162,226	1/1/75-12/31/75	8	20
Tennessee State University	210,806[2/]	3/1/74-8/31/75	5	14			5	14

MINORITY BIOMEDICAL SUPPORT GRANTS

Institution (by State)	1974 Awards				1975 Estimated Awards			
	Amount	Budget Period	Estimated Faculty/Staff	Estimated Student Participants[3/]	Amount	Budget Period	Faculty/Staff	Student Participants[3/]
Texas								
Bishop College	$ 45,526	1/1/74-12/31/74	3	6	$ 44,985	1/1/75-12/31/75	3	6
Pan American University	145,703	1/1/74-12/31/74	6	14	135,078	1/1/75-12/31/75	6	14
Texas A & I University	115,000[2/]	3/1/74-8/31/75	3	5			3	10
Texas Southern University	282,985	1/1/74-12/31/74	13	23	202,035	1/1/75-12/31/75	13	23
United Colleges of San Antonio	272,831	1/1/74-12/31/74	24	47	246,439	1/1/75-12/31/75	20	40
University of Texas at El Paso	105,022	1/1/74-12/31/74	14	25	106,833	1/1/75-12/31/75	14	25
Virginia								
Hampton Institute	79,070	1/1/74-12/31/74	5	12	71,200	1/1/75-12/31/75	5	9
Norfolk State College	105,679	1/1/74-12/31/74	7	12	99,526	1/1/75-12/31/75	7	12
Virginia State College	106,157	1/1/74-12/31/74	8	16	91,967	1/1/75-12/31/75	8	16
Virginia Union University	37,118	1/1/74-12/31/74	3	18	35,085	1/1/75-12/31/75	3	18
Virgin Islands								
College of the Virgin Islands	125,462[2/]	3/1/74-8/31/75	8	5			8	10
	$ 7,881,661		573	1,051	$5,980,594		571	1,041
The balance of $118,339 will be awarded during FY 1974 to ongoing grants for unanticipated increased costs.	118,339		It is estimated that eight new awards will be made from these FY 1975 funds.		1,289,406		99	118
	$ 8,000,000				$7,270,000		670	1,159

1/ Amounts approved by National Advisory Research Resources Council. Awards have not yet been made.

2/ These grants were funded from FY 1973 restored funds.

3/ Includes undergraduates, graduates and postdoctorals.

NON-NIH PROJECTS IN CENTERS

Mr. CONTE. Can a researcher use the facilities of a clinical research center if his support comes from a non-NIH source?

Dr. BOWERY. Yes, in fiscal year 1972 foundations, associations, voluntary State health chapters and industry provided some support for 628 biomedical research projects conducted in the general clinical research centers.

OUTPATIENT FACILITIES

Mr. CONTE. How many outatient facilities are supported under the clinical research centers program?

Dr. BOWERY. In fiscal year 1973 50 clinical research centers recorded a total of 34,579 outpatient visits. We estimate 53 centers will conduct 50,000 outpatient visits in fiscal year 1974. In addition we supported two exclusively outpatient biomedical research facilities at Johns Hopkins University and Vanderbilt University.

BIOTECHNOLOGY

Mr. CONTE. Under the biotechnology research program, is salary provided for service and other supporting personnel to maintain the complex kind of resources provided?

Dr. BOWERY. Yes.

Mr. CONTE. Is there any kind of obligation on the part of the institution with a biotechnology research award to share its facilities?

Dr. BOWERY. Criteria for being eligible for biotechnology resource support include the requirements that service be provided to users and collaboration with scientists outside the resource on a multicategorical basis be developed and maintained. Emphasis began last year in strengthening these services and collaborative activities of our specialized resources in order that their capabilities may be shared throughout the Nation.

USE OF PRIMATES

Mr. CONTE. Do you have any way of knowing how many investigators use the primate research centers?

Dr. BOWERY. Yes, the centers report yearly and last year there were 399 collaborative scientists conducting research in the centers. This is in addition to the 135 core scientists.

Mr. CONTE. Are there any primate species essential for research that you can't obtain at all from abroad anymore?

Dr. BOWERY. There are a number of primate species used in research in this country that are very difficult to obtain from abroad. An example would be the mystax marmaset from Peru and Brazil which is essential for hepatitis research.

Mr. CONTE. Does NIH have any direct monitoring responsibility to assure that rare animals are only used in research where necessary and are used carefully?

Dr. Bowery. NIH does not have any legal responsibility to monitor the use of rare animals; however, we do have a moral responsibility. The NIH initial review groups in reviewing grant and contract proposals also review the use of animals in the research activities. If the IRG or NIH staff determines that rare animals were not being properly used this would be called to the attention of the investigator.

Mr. Conte. Are there any primates necessary for research that can't be bred in captivity?

Dr. Bowery. There are a number of species of primates that are very difficult to breed in captivity. The primate rsearch centers have developed techniques for breeding many species of primates used in research but not all. For example, the owl monkey used in malaria research has proven to be very difficult to breed in captivity.

MINORITY BIOMEDICAL SUPPORT

Mr. Conte. Is any support given for graduate programs under the minority biomedical support program?

Dr. Bowery. Yes. In fiscal year 1973, 164 minority graduate students were supported by the MBS program. It is estimated that the same number wil be supported in fiscal year 1974.

Mr. Conte. Is that program providing training only for research careers or for careers in a wider range of health professions?

Dr. Bowery. Within the MBS program opportunities are provided for students and faculty to participate in biomedically relevant research projects. Through this involvement we hope that both will be stimulated to pursue advanced training leading to careers as investigators in biomedical research whether in clinical or other health-related science areas.

Mr. Conte. Are the planned eight new awards targeted for any special minority groups?

Dr. Bowery. The planned eight new awards for fiscal year 1974 are not targeted for any special minority groups. However, it is expected that by expanding eligibility to institutions with large numbers of minority students, but not necessarily a majority as previously required, and to American Indian reservations, that a number of applications will be received and awards will be made to the newly eligible institutions.

GENERAL RESEARCH SUPPORT GRANTS

Mr. Conte. With the abolishment of general research support grants, do you see any other alternatives of institutions to diluting research efforts or raising tuition?

Dr. Bowery. The availability of funds formerly provided under the general research support grant program through the project grant mechanism should provide the necessary funds for which institutions can compete.

BIOTECHNOLOGY

Mr. Robinson. With respect to your arrangements for computer-access networks related to research, would you supply for the record the institutions in Virginia, if any, which have this access, and, in general, the extent and nature of the use? It would be my assumption that the medical centers at the University of Virginia School of Medicine and the Medical College of Virginia would be participants.

Dr. BOWERY. At present no institutions in Virginia are directly associated with nationally shared computer resources sponsored by the biotechnology resources branch. However, opportunities for participation are available, up to the limit of personnel and hardware capabilities, to all qualified investigators throughout the Nation. These opportunities are made known through program announcements, a practice which will continue with increased emphasis in the coming years. Absence of participation at this time by scientists from any specific State undoubtedly reflects only that these shared resource arrangements are in their earliest stages of development and not any barriers to access.

ANIMAL RESOURCES

Mr. ROBINSON. In the matter of improved care of laboratory animals, I have been glad to note your report of progress. This is an emotional subject with many citizens, and Members of Congress receive considerable mail on the subject. It seems that horror stories persist, and I wonder if it would be useful to encourage institutions which are doing a good job in this respect to invite inspections by concerned groups? I realize, of course, that not all visitors would be satisfied with the precautions.

Dr. BOWERY. Your suggestion is good and is recognized by many institutions. These institutions have an open door policy for their animal facilities. This means that on an appointment basis individuals and groups may tour the facility. In addition, several animal facilities have scheduled open houses and invite the public in. Of course, portions of many animal facilities must be restricted as far as visitors are concerned either because the animals must be protected from catching diseases which might be carried by people or because the animals have been infected with human disease agents. Only employees, who are required to take special precautions, are allowed contact with such animals.

Mr. FLOOD. Thank you.

NATIONAL INSTITUTES OF HEALTH

Research Resources

Amounts Available for Obligation

	1974 Revised	1975
Appropriation	$133,472,000	$82,700,000
~~Amount withheld~~ (PL 93-192)	-5,153,000	--
Proposed supplementals *	-1,378,000	--
Subtotal, adjusted appropriation	126,941,000	82,700,000
Real transfer to:		
"Departmental management"	-6,000	--
(For Department-wide reductions in public affairs)		
Subtotal, budget authority (base obligations)	126,935,000	82,700,000
Unobligated balance, restored	2,196,000	--
Comparative transfer of restored unobligated balance from the following appropriations for General Research Support Grants:		
"National Cancer Institute	776,000	--
"National Heart and Lung Institute"	1,067,000	--
"National Institute of Dental Research"	780,000	--
"National Institute of Arthritis, Metabolism, and Digestive Diseases"	6,179,000	--
"National Institute of Neurological Diseases and Stroke"	4,137,000	--
"National Institute of Allergy and Infectious Diseases"	3,819,000	--
"National Institute of General Medical Sciences"	5,299,000	--
"National Institute of Child Health and Human Development"	2,950,000	--
"National Eye Institute"	1,170,000	--
"National Institute of Environmental Health Sciences"	372,000	--
"National Institute of Mental Health"	8,027,000	--
Total, obligations	163,707,000	82,700,000

* Including pay transfers

Summary of Changes

1974 Estimated obligations	$163,707,000
1975 Estimated obligations	82,700,000
Net Change	-81,007,000

	1974		Change from 1974	
	Pos.	Amount	Pos.	Amount
Increases:				
A. Built-in:				
1. Annualization of 1973 pay increase costs	--	--	--	$21,000
2. Within grade pay increase	--	--	--	18,000
3. FTS increase	--	--	--	15,000
4. Postage increase	--	--	--	6,000
5. BEC rate increase	--	--	--	1,000
6. One extra day of pay in 1975	--	--	--	6,000
7. DHEW-NIH General Expense Fund	--	--	--	15,000
8. Paymant to NIH Management Fund	--	--	--	14,000
Subtotal	--	--	--	96,000
B. Program:				
1. General clinical research centers	--	42,531,000	--	761,000
2. Biotechnology resources	--	11,923,000	--	386,000
3. Minority biomedical support	--	8,000,000	--	270,000
4. Fellowships				
a. Noncompeting	--	--	--	160,000
Subtotal	--	--	--	1,577,000
Total increases	--	--	--	1,673,000
Decreases:				
A. Program:				
1. General clinical research centers	--	42,531,000	--	-807,000
2. Biotechnology resources	--	11,923,000	--	-364,000
3. Animal resources	--	17,863,000	--	-929,000
4. General research support	--	78,826,000	--	-78,826,000
5. Minority biomedical support	--	8,000,000	--	-1,000,000
6. Fellowships				
a. Competing	--	--	--	-192,000
7. Training				
a. Noncompeting	--	--	--	-294,000
b. Competing	--	--	--	-68,000
8. Research and development contracts	--	1,580,000	--	-150,000
9. Research management and program services	72	2,532,000	--	-50,000
Total decreases	--	--	--	-82,680,000
Total, net change	--	--	--	-81,007,000

Explanation of Changes

Increases:

A. Built-in:

The total built-in increase of $96,000 will provide $21,000 for annualization of 1973 pay increase costs; $18,000 for within grade pay increases in 1975; $15,000 for use of the Federal Telecommunications System (FTS); $6,000 for increased postage costs; $1,000 for payment to Bureau of Employees Compensation; $6,000 for one extra day of pay in 1975; $15,000 for payment to the DHEW-NIH General Expense Fund; and $14,000 to the NIH Management Fund for centrally furnished services.

B. Program:

1. General clinical research centers--The program increase of $761,000 will provide funds for increased operating costs of approximately 83 general clinical research centers including research hospitalization (patient care) cost, personnel, supplies, and equipment.

2. Biotechnology resources--The program increase of $386,000 will provide for the increased cost for compliance with the DHEW policy of payment of full indirect cost.

3. Minority biomedical support--The program increase of $270,000 will provide funds for the support of several additional projects.

4. Fellowships--The amount of $160,000 reflects support for 10 noncompeting fellowship grants.

Decreases:

A. Program:

1. General clinical research centers--The decrease of $807,000 reflects the conversion of one competing grant to a noncompeting status.

2. Biotechnology resources--The decrease of $364,000 reflects the conversion of one competing grant to a noncompeting status.

3. Animal resources--The decrease of $929,000 includes an increase of: $223,000 for the Laboratory Animal Sciences program to cover the increased cost for compliance with the DHEW policy of payment of full indirect costs; a decrease of $362,000 for funding the seven primate research centers; and a decrease of $790,000 which includes $530,000 for the conversion of five competing grants to a noncompeting status and $260,000 for funding of the seven primate research centers.

4. General research support--The budget request reflects a decrease of $78,826,000 since no funds are requested for this program in 1975. The General Research Support Grant program which is designed to provide untargeted research funds to institutions to strengthen their biomedical research capacity, is of a lower priority than are program oriented research project activities. The NIH budget places a higher priority on maintaining financial and programmatic flexibility within the research project grant component of the NIH.

5. Minority biomedical support--The decrease of $1,000,000 reflects the reduced funding required in 1975 due to the funding of eight grants in 1974 for eighteen months.

6. Fellowships--The decrease of $192,000 reflects support for 14 competing fellowship awards converted to noncompeting status.

7. Training
   a. The decrease of $294,000 reflects the completion of two noncompeting training grants and reduced funding of four noncompeting training grants which will be on a phase out course with the 1975 budget.

   b. The decrease of $68,000 reflects the reduction for funding of a supplemental award in 1974 but not funded in 1975.

8. Research and development contracts--The decrease of $150,000 is a result of the termination of funding a contract for the Holloman Air Force Base Chimpanzee Breeding Colony.

9. Research management and program services--The total program decrease of $50,000 reflects reduction in travel, printing, renovation and other miscellaneous expense.

Obligations by Activity

Page Ref.		1974 Base *		1975 Estimate		Increase or Decrease	
		Pos.	Amount	Pos.	Amount	Pos.	Amount
	Special Programs						
182	Clinical research......	--	$41,724,000 (42,531,000)	--	$42,485,000	--	$761,000A/
185	Biotechnology research.	--	11,559,000 (11,923,000)	--	11,945,000	--	386,000B/
188	Laboratory animal sciences and primate research............	--	17,916,000 (18,941,000)	--	17,468,000	--	-448,000C/
192	General research support.............	--	45,250,000 (78,826,000)	--	0	--	-45,250,000D/
193	Minority biomedical support..............	--	7,000,000 (8,000,000)	--	7,270,000	--	270,000E/
195	Chemical biological information handling research............	--	1,000,000 (1,000,000)	--	1,000,000	--	0
197	Research management and program services.....	72	2,486,000 (2,486,000)	72	2,532,000	--	46,000F/
	Total obligations (bases).............	72	126,935,000 (163,707,000)	72	82,700,000	--	-44,235,000

* 1974 Base - Excludes 1973 appropriation restorations. Total obligations shown in parenthesis.

Explanation of Changes (by activity)

A/ Clinical research--The program increase of $761,000 will provide funds for increased operating costs of 83 general clinical research centers including research hospitalization costs, personnel, supplies and equipment.

B/ Biotechnology research--The program increase of $386,000 will provide additional funds for the increased cost for compliance with the DHEW policy of payment of full indirect cost.

C/ Laboratory animal sciences and primate research--The decrease of $448,000 includes an increase of $223,000 for the Laboratory Animal Sciences program for payment of full indirect costs of approximately $650,000; a decrease of $362,000 for the Primate Research program for funding the seven primate centers; a decrease of $150,000 for funding a contract with the Holloman Air Force Base Chimpanzee Breeding Colony; an increase of $62,000 for funding three additional fellowships; and a decrease of $221,000 for support of four training grants which will be on a phase out course with the 1975 budget.

D/ General research support--The budget reflects a decrease of $45,250,000 since no funds are requested for this program in 1975. The General Research Support Grant program which is designed to provide untargeted research funds to institutions to strengthen their biomedical research capacity, is of a lower priority than are program oriented research project activities. The NIH budget places a higher priority on maintaining financial and programmatic flexibility within the research project grant component of the NIH.

E/ Minority biomedical support--The program increase of $270,000 will provide support for several additional projects.

F/ Research management and program services--The increase of $46,000 for this program is the net of $96,000 for mandatory increases and reductions totaling $50,000 for miscellaneous expenses.

Obligations by Object

	1974 Estimate	1975 Estimate	Increase or Decrease
Total number of permanent positions......	72	72	--
Full-time equivalent of all other positions...........................	7	7	--
Average number of all employees.........	77	77	--
Personnel compensation:			
Permanent positions......................	$1,272,000	$1,297,000	$25,000
Positions other than permanent.........	58,000	60,000	2,000
Other personnel compensation...........	7,000	8,000	1,000
Subtotal, personnel compensation.....	1,337,000	1,365,000	28,000
Personnel benefits......................	150,000	151,000	1,000
Travel and transportation of persons.....	130,000	112,000	-18,000
Transportation of things................	5,000	5,000	--
Rent, communications and utilities.......	102,000	123,000	21,000
Printing and reproduction...............	50,000	40,000	-10,000
Other services..........................	673,000	697,000	24,000
Project contracts......................	1,580,000	1,430,000	-150,000
Supplies and materials..................	24,000	24,000	--
Equipment..............................	15,000	15,000	--
Grants, subsidies and contributions......	159,641,000	78,738,000	-80,903,000
Total obligations by object............	163,707,000	82,700,000	-81,007,000
Total obligations excluding 1973 appropriation.......................	126,935,000	--	--

Authorizing Legislation

Legislation	1975 Authorized	 Appropriation requested
Public Health Service Act, Title III, Part A, Section 301--Research and Investigation in general...	Indefinite	$82,700,000

Research Resources

Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
1965	$203,715,000	$202,959,000	$209,459,000	$209,759,000
1966 1/	103,919,000	105,169,000	110,469,000	105,669,000
1967	119,521,000	120,234,000	120,234,000	120,234,000
1968	142,841,000	142,841,000	156,141,000	142,841,000
1969	148,200,000	143,419,000	155,523,000	145,509,000
1970 2/	130,398,000	134,358,000	145,358,000	137,358,000
1971 3/	109,678,000	126,901,000	127,501,000	126,901,000
1972	117,269,000	127,160,000	136,648,000	135,648,000
1973*	99,013,000	135,767,000	143,694,000	135,767,000*
1974	88,626,000	133,316,000	133,994,000	133,466,000 4/
1975	82,700,000			

1/ Excludes the "National Institutes of General Medical Sciences" established as a separate appropriation in 1966.
2/ Excludes Office of International Research portions of which were transferred to the National Institute of Allergy and Infectious Diseases and the John E. Fogarty International Center.
3/ Excludes the Division of Computer Research and Technology incorporated into the "National Institutes of Health Management Fund" in 1971 and appropriation title changed to "Research Resources".
4/ Appropriation after reduction $126,935,000.

*Note: This appropriation authority was the continuing resolution. The appropriation amount was the House Allowance, which was the lower of the House or Senate amounts in the first vetoed bill.

Justification

Research Resources

	1974 Estimate		1975		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits..............	72	$1,487,000	72	$1,516,000	--	$29,000
Other expenses..............	--	125,448,000	--	81,184,000	--	-44,264,000
Total.............	72	126,935,000	72	82,700,000	--	-44,235,000

General Statement

The programs of the Division of Research Resources aid NIH in fulfilling its mission--to improve the health of all Americans--by providing for the development and support of specialized research settings for use by the grantees and contractors of the NIH categorical programs in the generation of new knowledge to hasten the progress of biomedical science in the treatment of human disease, and disability. Through the Division's five programs, (Clinical Research, Biotechnology Research, Laboratory Animal Sciences and Primate Research, Minority Biomedical Support, and Chemical Biological Information Handling Research) funds are awarded to the Nation's institutions of higher education, hospitals, and research organizations.

The research resources thus supported, whether clinical, animal, technological or human, have helped to insure that the research community possesses adequate tools, the necessary environment, and the continuity of support required for carrying out the targeted research missions which are supported by the categorical institutes of the NIH. These resources, which have been developed on an institutional, regional, or national basis, increase biomedical research productivity and opportunity by promoting and fostering interdisciplinary research endeavors which have led to the development of new knowledge directed toward the improved health of the American people.

DHEW - National Institutes of Health

CROSSWALK - 1974 COLUMN 1975 PRESIDENT'S BUDGET
(dollars in thousands)

INSTITUTE: Division of Research Resources

Program Mechanism	Research Grants Specials GRSG	Research Grants Specials Other	Training Programs Grants	Training Programs Fellowships	Research and Development Contracts	Other Direct Operations	Total
1974 Base Obligations							
1. Clinical Research..........	--	$41,724	--	--	--	--	$41,724
2. Biotechnology Research.....	--	11,329	--	--	$230	--	11,559
3. Laboratory Animal Sciences and Primate Research......	--	17,073	$296	$197	350	--	17,916
4. General Research Support...	$45,250	--	--	--	--	--	45,250
5. Minority Biomedical Support	7,000	--	--	--	--	--	7,000
6. Chemical Biological Information Handling......	--	--	--	--	1,000	--	1,000
7. Research Management and Program Service..........	--	--	--	--	--	$2,486	2,486
Subtotal................	52,250	70,126	296	197	1,580	2,486	126,935
Unobligated Balance Restored							
1. Clinical Research..........	--	807	--	--	--	--	807
2. Biotechnology Research.....	--	364	--	--	--	--	364
3. Laboratory Animal Sciences and Primate Research......	--	790	141	94	--	--	1,025
4. General Research Support...	33,576	--	--	--	--	--	33,576
5. Minority Biomedical Support	1,000	--	--	--	--	--	1,000
Subtotal................	34,576	1,961	141	94	--	--	36,772
Total Obligations............	86,826	72,087	437	291	1,580	2,486	163,707

DHEW - National Institutes of Health

CROSSWALK - 1975 COLUMN 1975 PRESIDENT'S BUDGET
(dollars in thousands)

INSTITUTE: Division of Research Resources

Program Mechanism	Research Grants Specials GRSG	Research Grants Specials Other	Training Programs Grants	Training Programs Fellowships	Research and Development Contracts	Other Direct Operations	Total
1. Clinical Research..........	--	$42,485	--	--	--	--	$42,485
2. Biotechnology Research.....	--	11,715	--	--	$230	--	11,945
3. Laboratory Animal Sciences and Primate Research......		16,934	$75	$259	200	--	17,468
4. General Research Support...	--						--
5. Minority Biomedical Support	$7,270	--	--	--	--	--	7,270
6. Chemical Biological Information Handling......	--	--	--	--	1,000	--	1,000
7. Research Management and Program Service..........	--	--	--	--	--	$2,532	2,532
Total Obligations............	7,270	71,134	75	259	1,430	2,532	82,700

Research Resources

Budget Mechanism

	1974*		1975	
	Number	Amount	Number	Amount
Grants				
Special				
General Research Support	490	$52,250,000	67	$7,270,000
General Clinical Research Centers	82	41,724,000	83	42,485,000
Biotechnology Resources	55	11,329,000	46	11,715,000
Animal Resources	93	17,073,000	83	16,934,000
Total Grants	720	122,376,000	279	78,404,000
Fellowships				
Non-competing	6	57,000	16	217,000
Competing	--	--	--	--
New	10	140,000	3	42,000
Supplemental	--	--	--	--
Subtotal	16	197,000	19	259,000
Training Grants				
Non-competing	6	228,000	4	75,000
Competing	--	--	--	--
New	--	--	--	--
Supplemental	1	68,000	--	--
Subtotal	7	296,000	4	75,000
Research and Development Contracts	18	1,580,000	17	1,430,000
Research Management and Program Services	--	2,486,000	--	2,532,000
TOTAL	761	126,935,000	319	82,700,000

* Excludes 1973 appropriation restorations.

Clinical Research

Authorizing Legislation: (Public Health Service Act, Title III, Part A)

	1974 Base *		1975		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits...............	--	--	--	--	--	--
Other expenses..............	--	$41,724,000	--	$42,485,000	--	-$761,000
Total.............	--	41,724,000	--	42,485,000	--	-761,000
Budget Mechanism:						
Research Grants:						
Special..................	--	41,724,000	--	42,485,000	--	-761,000

* Excludes 1973 appropriation restorations.

Introduction:

The Clinical Research program provides the Nation's leading clinical investigators with the specialized resources and facilities necessary to close the gaps in medical knowledge and translate the latest laboratory discoveries into improved treatment and care for patients. This is accomplished by intensive patient-oriented investigations made possible by the Clinical Research program. Investigations within the general clinical research centers cover the entire spectrum of medical disease involving such areas as cancer therapy, transplantation, obesity, population control, human growth and metabolism, heart disease, high blood pressure, and mental retardation. In these centers the latest conceptual and technical advances from basic science and animal research are developed into refined tools to better understand and treat human disease. Although much medical research can be conducted on laboratory animals eventually it must progress to the clinical level, where studies are conducted on human subjects. It should be noted that human subjects are also essential for studying those diseases and biological processes which are not duplicated in any other living creature.

Approximately two-thirds of all research hospital beds supported by the NIH in the Nation and used for research on human subjects are funded by this program.

The general clinical research centers supported through this program are physically discrete research units located in university affiliated hospitals. Traditionally support is provided for a fixed number of beds staffed by specially trained nursing, dietary, and laboratory personnel directed by a physician.

A clinical research center consists of from four to 30 beds, the average being 11. It might be said that each center is a special miniature research hospital consisting of bedrooms, bathrooms, treatment rooms, core laboratories, metabolic diet kitchens, patients' lounge, nurses' station and conference rooms.

Although most of the "general" centers can accommodate both adults and children, approximately 20 percent of the centers focus on pediatric problems. Also, a few have been built around premature infants, maternal-child and acute surgical problems.

The original concept of a center as a geographically and physically discrete inpatient unit has been extended to include facilities and personnel necessary to incorporate an outpatient clinical research program. All of the centers have been allowed the option of modifying their current facilities in order to facilitate the increased use of ambulatory patients as research subjects.

Program Plans 1975:

The amount requested for fiscal year 1975 will provide support for approximately 83 general clinical research centers, including funding of approximately 840 beds. The funds will provide for the operating costs of a center, including research hospitalization (patient care) cost, personnel, supplies and equipment. In the case of a new center, renovation costs as required are provided. The decrease in the number of beds supported in 1975 is due to the pressure of inflationary costs.

1973 Accomplishments:

Approximately 12,000 individuals are involved with the clinical centers. The center grants provide salary support for 1,800 center personnel which includes 126 physicians, 1,041 nurses, 227 laboratory personnel, and 20 recreational and occupational therapists. In addition to the program supported staff, there are over 2,400 clinical investigators receiving support of $108,000,000 in NIH grants and contracts and more than 600 grants from industry and private foundations currently supporting medical research projects at the centers. In addition to the centers' staffs, patients and clinical investigators, 7,746 individuals participated in the centers' activities during 1973, including 1,564 resident physicians, 460 dietetic interns, 2,910 medical students, 748 interns, 1,120 fellows, and 944 student nurses.

Clinical investigations conducted under this program are diverse and supportive of biomedical research carried out in many categorical disease areas and are demonstrated by the following examples:

Hematology

Sickle cell anemia is a widespread disorder among the black population in this country. To date, therapy has been mostly symptomatic and despite early promises of other successful medications there has been no truly effective treatment which can prevent the sickling of these patients' cells. Workers at Rockefeller University have found that cyanate can affect the hemoglobin molecule involved in sickle cell anemia in a way that impairs sickling. They have done extensive studies of this chemical in animals to determine its efficacy and side effects, and are now undertaking clinical trials to determine its use both orally, and taken by vein, in patients with sickle cell anemia. A major complication in sickle cell anemia is the development of infections. Investigators at Yale University found that individuals with this disorder have a functional lack of a spleen and this finding may be of relevance in the propensity of these individuals to develop serious infections.

In another anemia, thalassemia, otherwise known as Mediterranean anemia, survival time of red cells is markedly shortened and severe chronic anemia develops. Invalidism with its profound psychological impact on both child and family is followed by death, often by the second decade of life. The only known treatment for this condition is transfusion, which increases the oxygen carrying capacities of the blood. A study under way in a Clinical Research Center in which children are given enough blood to maintain near or normal hemoglobin levels at very frequent intervals, has found that these children maintain a relatively normal level of activity and have not thus far shown the signs of chronic iron poisoning in the degree characteristic of children treated in the conventional way. Changes in psychological state of both the child and his parents have been striking and reflect the real changes in the physical state of the patient.

Corneal Transplant - Ophthalmology

Corneal transplantation has been a remarkable advance to provide vision to patients whose corneas have opacified to the extent that they can no longer see. However, there have been many problems involved in this procedure, among them rejection of the transplanted cornea. In a study at Boston University, it has been found that a postoperative course of Imuran and steroids provided greatly increased success rates for this operation. A randomized study of these drugs is now planned to accurately determine their place in corneal transplantation.

Renal Disease

To better understand the pathogenesis of kidney diseases, doctors at the Peter Bent Brigham Hospital have explored the distribution of kidney blood flow using radioisotope techniques. It has been determined that there are alterations in kidney blood flow in various types of renal failure and it is hoped that treatment for these disorders will be improved through understanding of these abnormalities in blood flow.

The area of renal transplantation has brought new hope to patients with previously incurable kidney diseases. Doctors at the University of Minnesota Clinical Research Center are presently working in this area to understand, and to treat or prevent, naturally occurring immunologic renal diseases in man and to determine which classes of renal diseases might benefit from renal transplantation. In the course of these studies, these investigators have studied the world's largest collection of renal transplants in diabetics.

In another major means of palliating kidney disease, investigators at the University of Utah have developed a new technique in maintenance hemodialysis which obviates one of the most bothersome problems in this therapy--namely, the placement of a second needle for the dialysis. In other studies there, a new artificial kidney has been developed which utilized a disposable insert. This is important since these new machines cost about one-third the price of the units currently in use.

Immunology

At the University of Minnesota Clinical Research Center, doctors successfully treated leprosy by immunotherapeutic methods. Dramatic clinical improvement was shown in a dozen leprosy cases by creating an immunologic attack against a drug-resistant disease. Similar studies on the center at the University of Rochester now give hope to approximately 15 to 50 million lepers in the world who are resistant to drug treatment. This new treatment also opens new research parameters in the use of thymus-type white cells against disease.

Program Plans 1974:

The funds available in 1974 will provide continued support for 81 centers and the establishment of one new center totaling approximately 882 beds. Grants are awarded in yearly increments for a project period of three to five years. The average grant is approximately $500,000 yearly.

Biotechnology Research

Authorizing Legislation: (Public Health Service Act, Title III, Part A)

	1974 Base *		1975		Increase or Decreases	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits..............	--	--	--	--	--	--
Other expenses..............	--	$11,559,000	--	$11,945,000	--	$386,000
Subactivities:						
Biotechnology Research.....	--	11,329,000	--	11,715,000	--	386,000
Research and Development Contracts...............	--	230,000	--	230,000	--	--
Total...............	--	11,559,000	--	11,945,000	--	386,000
Budget Mechanism:						
Research Grants:						
Special.................	--	11,329,000	--	11,715,000	--	386,000
Research and Development Contracts............	--	230,000	--	230,000	--	--
Total............	--	11,559,000	--	11,945,000	--	386,000

* Excludes 1973 appropriation restorations.

Introduction:

The Biotechnology Research program awards grants and contracts for the development and use of sophisticated health-related technologies. Emphasis is placed on digital computation, mass spectroscopy, nuclear magnetic resonance spectroscopy, and electron microscopy, although other technologies also are included to a limited degree. The main thrust of this program is the furtherance of biomedical research through creation of centers of technological excellence which in turn provide the grantees and contractors of NIH's categorical programs with investigative opportunities they otherwise would not have.

The nature and scope of the various biotechnology resources over the years have been closely associated with major technological advances and research opportunities. Beginning from almost pure research service activities ten years ago, the Program has evolved to the point where, in addition to furnishing research services, each resource now in its own specific area of technology enters into close collaborative activities with its user community; engages in core research to further develop the technology as a tool in biomedical research; and conducts formal and informal training to acquire new skills for its own staff and to disseminate the benefits of its technology to the user community. Incorporating all of these activities within a resource makes the resource more responsive to the needs of the medical scientific community.

Program Plans 1975:

The amount requested for FY 1975 will provide for continued support for 46 biotechnology research resources which includes payment for full indirect costs and biotechnology contract activities.

Program capabilities:

Biomedical research activities dependent upon these resources are:

Computer Sciences and Technology:

--monitor and predict, through models, potential faults in life-support equipment such as is found in cardiopulmonary intensive care units

--place major discrete health care and clinical research functions such as radiation treatment planning and nuclear medicine applications under nearly comprehensive computer control

-- provide routine on-line control of laboratory experiments

-- extend the investigator's ability to cope with vast and complex data through direct interaction with computers

-- facilitate the introduction of mini-computers into specialized research applications

-- permit the biochemist to translate his data easily into readily recognizable graphic form instead of being forced to deal with it in numerical form

Nuclear Magnetic Resonance Spectroscopy:

--examine enzymes in sufficient detail to determine the three-dimensional structural features that are necessary for biological activity

Mass Spectroscopy:

--analysis of extracts of the inner walls of human arteries from patients suffering from arteriosclerosis leading to the identification of a number of components in deposits resulting from this disease

--identification of toxic agent(s) in patients comatose and near death from drug overdose and in elucidating how and where drugs, environmental chemicals and the like are modified and transformed by the body to produce yet other molecules whose effects may be damaging

Initiatives in Research Resource Sharing:

The evolution of the Biotechnology Research Program has produced an array of diverse resources, all designed to meet one or more specific technological needs of biomedical scientists. As new, advanced technological tools are shown to be relevant to health research, the Program experiences demands to make these tools available to the biomedical community. Because most of the new technologies are more sophisticated and costly than their predecessors, the emerging resources are more complex and require a more highly specialized technical staff for their maintenance, successful operation, and application to relevant health problems. Moreover, because these resources are devoted more to specific research needs, they are usually able to make a more meaningful contribution to the activities of their clientele than would be possible in a general-purpose type of activity.

The demand for these costly specialized resources has required that support be shifted from resources which exclusively serve scientists in their host institutions to national resources which serve scientists residing throughout the country. The establishment of nationally shared resources is believed to be a scientifically rational and fiscally realistic way to promote and sustain the broad availability of sophisticated research tools required by modern biomedical research. A summary of some of the actions underway and envisioned for FY 1975 is given below.

High Voltage Electron Microscopy Resources:

A National High Voltage Electron Microscopy (HVEM) Program: Two microscopes are now available to qualified scientists irrespective of geographical location or institutional affiliations. The establishment of the HVEM resources as national facilities is the first effort of the Biotechnology Research program in its Resource Sharing Program. This joint effort will give the Nation's biomedical scientists a broader range of opportunities for employing HVEM than any one resource could realistically do alone.

The National HVEM program was expanded in FY 1973/74 to include resources in related areas, giving an ensemble of activities specializing in the application of electron optics to biomedical problems. The other resources in this group are a unique scanning transmission electron microscopy resource and an electron microprobe resource. Further elaboration, broader use and thorough evaluation of this ensemble constitutes the agenda for FY 1975.

Biomolecular Characterization Resources:

During FY 1973/74 the Biotechnology Research program began to promote resource sharing as a means of maximizing the application of mass spectrometry and nuclear magnetic resonance spectroscopy to biomedical research. The results of a contract-supported study that examined the service component of the Mass Spectrometry Resources Program demonstrated that one laboratory, under proper management, could effectively meet the mass spectrometry service requirements of clinicians, pharmacologists, biochemists, and medicinal chemists located throughout a large geographical area. Ongoing resources were encouraged to expand their user communities and increase their inter-institutional commitments, and several new centers were established.

Program Plans 1974:

During 1974 continued support will be provided to 55 biotechnology research resources and biotechnology contract activities. Included in the contract activities is the CLINFO project. The CLINFO project is a scientific inquiry, sponsored by the Division of Research Resources (DRR) of the NIH, that is aimed at identifying and characterizing the intellectual tasks and the information flows in clinical investigation (medical research directly involving human subjects) and at developing methods for facilitating these tasks and flows.

Laboratory Animal Sciences and Primate Research

Authorizing Legislation: (Public Health Service Act, Title III, Part A)

	1974 Base *		1975		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits...............	--	--	--	--	--	--
Other expenses..............	--	$17,916,000	--	$17,468,000	--	-$448,000
Total.............	--	17,916,000	--	17,468,000	--	-448,000
Subactivities:						
Laboratory Animal Sciences and Primate Research....	--	17,073,000	--	16,934,000	--	-139,000
Fellowships..............	--	197,000	--	259,000	--	62,000
Training.................	--	296,000	--	75,000	--	-221,000
Research and Development Contracts..............	--	350,000	--	200,000	--	-150,000
Total............	--	17,916,000	--	17,468,000	--	-448,000
Budget Mechanism:						
Research Grants:						
Special................	--	17,073,000	--	16,934,000	--	-139,000
Fellowships..............	--	197,000	--	259,000	--	62,000
Training.................	--	296,000	--	75,000	--	-221,000
Research and Development Contracts..............	--	350,000	--	200,000	--	-150,000
Total............	--	17,916,000	--	17,468,000	--	-448,000

* Excludes 1973 appropriation restorations.

Introduction:

The Laboratory Animal Sciences and Primate Research program assists institutions in providing animal resources for biomedical research and special research environments where scientists can conduct biomedical and behavioral research using nonhuman primates and other animals. It also provides training grants and fellowship support in laboratory animal science and medicine to assure a continuing supply of research support personnel.

Program Plans 1975:

The FY 1975 budget will provide for the support of 76 Laboratory Animal Science Projects and seven Primate Research Centers; four contract supported projects; 19 fellowships and four training programs (about five trainees).

Laboratory Animal Science

Project grants in Laboratory Animal Science provide support for resource colonies of well-defined animals which possess unique or special characteristics for use in a variety of biomedical research areas. These colonies provide essential animal subjects and materials to 151 NIH research project grant activities (total annual funding of $9,871,000) and 125 research projects supported by other sources (total annual funding of $2,747,000). Examples of research using these special resource colonies include: studies of chronic alcoholism and associated liver degeneration in miniature swine; investigations using "fatty" rats to detect changes in metabolism and growth associated with obesity; research on mink with an inherited disease similar to muscular dystrophy; study of lemmings, a form of Alaskan rodent, for heart disease, diabetes and problems associated with milk-producing glands; and studies of lactose intolerance (an enzyme alteration that results in inability to properly digest milk) using squirrel monkeys.

Laboratory Animal Science grants also support 16 animal disease investigative laboratories. These laboratories are instrumental in controlling disease in large animal research colonies. Some of the diseases of animals they seek to control are also valuable in relation to the study of human disease. For example, cancer of the colon was detected in a colony of mice at Yale University Medical School. This model can now be used to study human large bowel cancer and its treatment. Another feature of the Laboratory Animal Science program is that of assisting institutions to improve their animal facilities and resources to meet the requirements of the Animal Welfare Act of 1970 (P.L. 91-579) and HEW policies on the care and treatment of laboratory animals. About thirty-five institutions will receive this type of animal resource improvement support during 1974. These awards typically support establishment of central administration and uniform high standards for animal care; training and employment of professional and technical experts in research animal care; and improved physical facilities and equipment.

Laboratory Animal Science grants also support information and reference centers to make efficient use of animals in research; research projects to gain information for disease control and environmental requirements of laboratory animals; and institutional primate colonies.

Support for research training is made to institutions and individuals through training and fellowship grants. These grants provide for continued education of individuals at the postdoctoral level by training specialists in the fields of laboratory animal medicine. These grants prepare individuals to provide professional care to many species of laboratory animals, to manage central animal resources and to give special assistance to investigators through their superior knowledge of animal biology and understanding of research methods. The individuals receiving additional training are prepared to participate in the teaching of graduate students and new investigators and to pursue their own research interests either as independent investigators or members of a research team. About 13 individuals complete the two to three year training period annually. This is a critically short area and open positions generally outnumber the people available to fill them in a ratio of two to one.

Primate Research

The Primate Research Centers portion of the program supports seven regional centers which provide special research environments where biomedical research in a number of important areas is being conducted. These Centers continue to provide leadership in the expanding field of medical primatology; and each year, numerous contributions are made in the areas of reproductive biology and population control, cardiovascular disease, infectious diseases, and neural and behavioral disorders. In addition, two smaller specialized primate resource programs are supported. In total, 120 core staff scientists conduct research on 125 grants and contracts. As a result, a total of 608 scientific reports were published last year. In addition, about 400 collaborative scientists from a number of universities utilized these facilities to conduct their research; and 375 scientists were provided with biological specimens. The Centers are active in both technical and research training, and a total of 136 graduate students participate in research activities as part of their training. The Centers maintain colonies of some 7,700 primates representing 45 species.

Examples of recent research findings from the Primate Centers include the following:

Effects of marihuana on social behavior and endocrine systems

The long-term effects of heavy daily intake of marihuana on social behavior and stress-response hormones are being studied at the California Primate Center. Treatment will be continued for a year or longer to demonstrate whether long-term drug effects will include slowly-developing basic changes in personality or emotional responsitivity, and in reproductive and sex hormones as well as stress-response hormones. Such effects now appear likely, counter to popular opinion at the beginning of the study.

Serum Hepatitis

Serum hepatitis has been an increasing health problem over the past decade, especially for patients requiring frequent blood transfusions. Until recently, research was hampered because no laboratory animal which could be infected with the hepatitis agent was known.

At the Delta Regional Primate Research Center, Covington, Louisiana, three chimpanzees inoculated with viral materials from human patients exhibited signs of serum hepatitis. The course of the infections in the chimpanzees was similar to that seen in man, reaffirming the findings of other laboratories that the chimpanzee is the best available model for studying this very debilitating disease in man. The Center's role is to try to determine the relative virulence of the various subtypes of serum hepatitis.

The Effect of PCB

The use of polychlorinated biphenyls (PCB's) in industrial processing and plastic consumer products was restricted in 1970 when it became apparent that these chemicals, known to be toxic, were becoming widespread in the environment. These compounds are very stable and can be expected to persist and accumulate in the fatty tissues of animals and man. Levels have been set for the amounts of PCB's allowable in human food; recently, these levels were revised downward.

The Oregon Primate Center has found that young rhesus monkeys, consuming food containing commercial PCB's at levels to the allowable limits, sicken and die in four to six months. On postmortem examination, evidence of abnormalities were found in sebaceous skin glands, hair, liver, and lining of the stomach.

Seafood Poisoning

In 1972, about 500 of 1,200 participants at a shrimp cookout in Covington, Louisiana became ill. The bacteriologist at the Delta Regional Primate Research Center was asked to help determine the cause. He discovered the little-known bacterial organism, Vibrio parahaemolyticus. There is no reliable way to distinguish harmless and disease-producing strains of this organism, but Center scientists have found that the strains which cause diarrhea in man provoke the same effect in the rhesus monkey. Final results of the study may shed more light on the life-cycle of this pathogenic micro-organism and lead to a relatively rapid test to determine possible contamination.

Primate Supply

The entire program has put increased emphasis on domestic breeding of primates. Destruction of natural primate habitats and the desire of exporting countries to avoid over-exploitation of natural resources and wildlife is leading to critical problems in the supply of primates.

For example, India has reduced the number of rhesus monkeys it will allow to be exported by 40 percent. Rhesus monkeys are the most commonly used primate. Nonhuman primates are essential to over 1,000 NIH research project grants and are very important in testing the safety of polio vaccine and other drugs and vaccines. The Primate Centers breed many of the animals they need (about 1,000 per year) and other projects in the program breed several hundred more. In total, however, only about five percent of the primates used nationally are bred domestically. The Program expects to increase its investment in primate breeding by about 20 percent in FY 1975. An added bonus of domestic primate breeding will be a higher quality animal.

Program Plans 1974

The FY 1974 budget will provide for the support of 86 Laboratory Animal Science Projects; seven Primate Research Centers; six contract supported projects; 16 fellowships and seven training programs (about 21 trainees).

General Research Support

Authorizing Legislation: (Public Health Service Act, Title III, Part A)

	1974 Base *		1975		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits...............	--	--	--	--	--	--
Other expenses...............	--	$45,250,000	--	--	--	-$45,250,000
Total..............	--	45,250,000	--	--	--	-45,250,000
Budget Mechanism:						
Research Grants Special..................	--	45,250,000	--	--	--	-45,250,000

* Excludes 1973 appropriation restorations.

Introduction:

The General Research Support Grant Program was started in 1962 after the passage of Public Law 86-798. Within broadly defined guidelines, funds awarded to institutions engaged in health-related research may be spent for direct costs of health research in any way deemed appropriate by the recipient institution.

Viewed as complementary to categorical project grants this grant program provided funds on a continuing basis to eligible institutions for their self determined flexible use in support of biomedical research and research training activities. The amount of each award is based on the total of the National Institutes of Health and the National Institutes of Mental Health research project grants received by each institution in the preceding fiscal year. Eligible institutions include schools of medicine, dentistry, osteopathy, public health and other types of health professional schools, hospitals, state and local health departments, non-academic health research organizations, and non-health related academic institutions.

Program Plans 1975:

No funds are requested for this program in 1975 since the General Research Support Grant Program, which is designed to provide untargeted research funds to institutions to strengthen their biomedical research capacity, is of a lower priority than are program oriented research project activities. The NIH budget places a higher priority on maintaining financial and programmatic flexibility within the research project grant component of the NIH.

Program Plans 1974:

The funds available in FY 1974 will provide support to approximately 423 awardees.

Minority Biomedical Support

Authorizing Legislation: (Public Health Service Act, Title III, Part A)

	1974 Base *		1975		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits...............	--	--	--	--	--	--
Other expenses...............	--	$7,000,000	--	$7,270,000	--	$270,000
Total.............	--	7,000,000	--	7,270,000	--	270,000
Budget Mechanism:						
Research Grants:						
Special.................	--	7,000,000	--	7,270,000	--	270,000

* Excludes 1973 appropriation restorations.

Introduction:

The Minority Biomedical Support (MBS) Program started in FY 1972 by the Division of Research Resources was designed to strengthen the institutional health related research capabilities of four-year colleges, universities and health professional schools in which student enrollments are drawn mainly from ethnic minority groups. It constitutes the major focus and concentrated effort of the NIH to involve minority institution scientists in biomedical research and to expose minority students to the challenges and opportunities in biomedicine.

This program was initiated, at the encouragement of the Senate Appropriations Committee, in order that minority groups may have equality of opportunity to become investigators in biomedical research.

Since the MBS Program was modeled after no other program within NIH, it is unique and therefore has been experimental and changing in nature. Consequently, the program has been improved as need for modification has been gained through experience.

The program provides institutional support for biomedical research and research training. Specifically the purpose of the Minority Biomedical Support Program is to:

- Enhance the biomedical research and training environment of minority institutions
- Strengthen the research facilities of minority institutions
- Involve minority students in research
- Increase the number of minorities well trained for health professional and graduate schools

Program Plans 1975:

...

In 1975 the funds requested will provide support to 59 continuing awards and approximately eight new awards.

Accomplishments 1973: In 1973, of the 38 institutions that received support in 1972, 36 received second year support based on prior commitments. Second year awards, reflecting increased program momentum, were made at higher levels than in the initial year. In addition, 15 other institutional components received awards, including one renewal and 14 new.

Program Plans 1974: Currently, 52 MBS awards are active involving 58 colleges and universities with predominantly ethnic minority student enrollments. They consist of 45 "Black", 11 "Spanish-speaking", one "Hawaiian", and one "American Indian" institution located in the District of Columbia, Puerto Rico, and 20 states.

During the first two years of the program 398 faculty, 648 undergraduate, and 115 graduate students received support for research and research training.

The number of minority faculty and students supported by the program is expected to increase in 1974 by almost 14 percent to 1,314 persons, a number that is in marked contrast to the small number engaged in biomedical research in 1971 prior to the establishment of the MBS Program. Many of these MBS students are expected to pursue doctorate degrees.

During FY 1974 the program is being gradually modified to include four-year colleges where there are large numbers of minority (i.e., Black, Spanish-Speaking, American Indian, or Oriental) students, but not necessarily a majority (as required under the original MBS program guidelines.) There are also a few junior colleges and community colleges where there are large numbers of minority students enrolled. By including these institutions and others such as the American Indian Tribal Councils, the program could reach a considerable number of minorities, including Spanish speaking people and American Indians, as well as many Blacks, who were originally excluded from the program. The desirability and feasibility of such changes in institutional eligibility is being closely followed. In 1974 the amount available will allow for continuing commitments to 51 institutions and approximately 8 new awards.

Chemical Biological Information Handling Research

Authorizing Legislation: (Public Health Service Act, Title III, Part A)

	1974 Base *		1975		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits...............	--	--	--	--	--	--
Other expenses..............	--	$1,000,000	--	$1,000,000	--	--
Total.............	--	1,000,000	--	1,000,000	--	--
Budget Mechanism:						
Research and Development Contracts................	--	1,000,000	--	1,000,000	--	--

* Excludes 1973 appropriation restorations.

Introduction:

The Chemical Biological Information-Handling (CBIH) Program is an NIH-initiated and NIH-directed effort concerned with computer tools for drug research. The heart of this program is a unique computer system called PROPHET. The long-range goal for PROPHET is to accelerate the growth of predictive science regarding drugs and drug-related phenomena. The immediate objective is to facilitate a broad spectrum of laboratory and clinical investigation concerned with how chemical substances influence--and are influenced by--life processes. The CBIH Program seeks to fulfill both of these purposes by making PROPHET's powerful information-handling capabilities available to individual scientists throughout the Nation in a convenient and easy-to-use form and by encouraging computer-mediated sharing of data, programs, and the like among them.

The PROPHET System hardware and software complex is the result of over five years of effort by contractors, advisors, and staff of the CBIH Program. The hardware is a large, time-shared, digital computer. The software is an extensive array of highly integrated special purpose programs. A PROPHET user has access to the System remotely via a TV-like display terminal communication over telephone lines.

The PROPHET System has five features that jointly set it apart from other research computer systems:

1. It is established as a national resource especially for the community of scientists concerned with chemical/biological interrelationships.

2. It can be mastered readily by scientists who have little or no prior computer experience.

3. It can be applied effectively to a wide range of complex information-handling tasks relevant to chemical/biological interrelationships without the user having to write any computer programs.

4. It can accommodate very sophisticated users/programmers, integrating user-prepared procedures automatically into the basic system.

5. Through the medium of a set of standard logical frameworks (called data types) for organizing experimental data, molecular structure descriptions, and the like, it seeks to promote the sharing of information among users.

The PROPHET project is the first and only case where a community of geographically dispersed pharmacologists has shared a research tool of such scope and power, and the years immediately ahead offer a unique opportunity to catalyze the discovery, communication, and use of new pharmacological knowledge.

Implementation of this program is exclusively through contracts with profit-making organizations, universities, and other Federal agencies.

Program Plans 1975:

The FY 1975 funding has three objectives: (a) to enlarge the number of scientists using the PROPHET System, (b) to refine PROPHET's capabilities and operational efficiency, and (c) to undertake never-before-possible experiments in computer-mediated scientific communications involving the mechanisms of drug action. The absence of a budget increment will require that work toward objective "b" be reduced by about 1 man-year of effort from previous years in order to compensate for the effect of inflation on labor costs. Also, it is the intent of the CBIH Program to have the PROPHET users begin sharing in the continuing costs of operating the service.

Program Plans 1974:

FY 1973 marked a major milestone in the evolution of the CBIH Program. During this year the PROPHET System emerged after over five years of intensive NIH-directed design and development to become a service to more than 30 laboratory and clinical investigators at 4 terminal installations in 3 states. Moreover, as a result of a national competition conducted by the Program, another 10 sites (out of 28 applying)--with, conservatively estimated, up to 80 potential additional user-scientists--have been identified and await access to PROPHET's services. By the end of FY 1974 it is planned that there be 6 user sites and approximately 65 users. By the end of FY 1975 the target numbers of sites and users are 10 and 100, respectively.

Research Management and Program Services

Authorizing Legislation: Public Health Service Act, Title III, Part A

	1974 Base *		1975		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits...............	72	$1,487,000	--	$1,516,000	--	$29,000
Other expenses..............	--	999,000	--	1,016,000	--	17,000
Total..............	72	2,486,000	72	2,532,000	--	46,000
Budget Mechanism:						
Research Management and Program Services....	72	2,486,000	72	2,532,000	--	46,000

* Excludes 1973 appropriation restorations.

Introduction:

This activity provides overall administrative management, scientific direction and coordination of the Division's programs. Funds are used for salaries and related cost for staff of the immediate Office of the Director, which includes administrative services, financial management, program planning; the Program Analysis Branch, and for staff necessary for program planning and development, and review and evaluation of grant and contract programs.

Program Plans 1974 and 1975: In 1975, the Division will be involved in a number of activities designed to broaden and expand the impact of its programs. Among these are: (1) the continued evaluation of the Minority Biomedical Support Program to determine the feasibility of its expansion to include other institutions and organizations, such as two-year colleges, where a significant number of minority students are enrolled but where they do not constitute a majority of the student body; (2) further develop the research resource sharing concept to enable institutions which require sophisticated technology in order to conduct their research, but where the volume of research does not justify separate large and complex resources, to share existing resources of other institutions; and (3) the development of new management and organizational concepts within the Division designed to more effectively serve the biomedical research community.

The funds requested in FY 1975 will provide continued support for this program. This amount includes funds for the mandatory increases including within grade increases, postage and FTS rate increase, one extra day of pay, and for the NIH Management Fund for centrally furnished services.

During 1974, this activity continued to provide the overall direction and administration of the Division's programs.

NATIONAL INSTITUTES OF HEALTH

Research Resources

Program Purpose and Accomplishments

Activity: Clinical Research (Public Health Service Act, Title III, Part A)

1974			1975	
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
--	$41,724,000	Indefinite	--	$42,485,000

Purpose: The Clinical Research Program meets a Nation-wide need for specialized facilities by providing clinical research opportunities and resources to large numbers of investigatory and research groups to study human disease. The clinical centers, which are physically discrete hospital units usually located in university-affiliated hospitals, provide essential bed space, laboratory equipment and trained staff necessary for such research. In these centers the latest conceptual and technical advances from basic science and animal research are developed into refined tools to better understand and treat human disease.

Explanation: Applications for grant awards are submitted by institutions to the General Clinical Research Center program. Applications are reviewed by the General Clinical Research Centers Advisory Committee, program staff and the National Advisory Research Resources Council. Priorities of awards are determined by staff upon recommendation of the National Advisory Research Resources Council and are based upon the nature of the proposed research described in the application. The Clinical Research Program grants are awarded in yearly increments for a project period of three to five years. There are no matching fund requirements.

Accomplishments in 1974: During 1974 the program supported 82 clinical research centers in roughly two-thirds of the teaching medical institutions of the nation. Although these centers can accommodate both children and adults, 20 percent of them focused on pediatric problems. The original concept of a center as a geographically and physically discrete inpatient unit has evolved in response to the changing needs of the Nation's clinical investigators. This concept is now being extended beyond the research limitations of a solely inpatient unit to include facilities and personnel necessary to incorporate an outpatient or ambulatory clinical research program. In recognition of this change, all existing centers have been allowed the use of ambulatory subjects as research patients. Presently a limited amount of research on outpatients is being conducted in 47 centers, and one exclusively outpatient center is operational.

Areas of emphasis included research in carbohydrate and fat metabolism as related to atherosclerosis and causes and treatment of high blood pressure, the causes and treatment of diabetes, and major emphasis on growth and development.

Objectives for 1975: In 1975 the funds requested will provide continued support to approximately 83 clinical research centers including funds for approximately 840 beds. The funds provide for the operating costs of a center, including research hospitalization (patient care) cost, personnel, supplies and equipment.

NATIONAL INSTITUTES OF HEALTH

Research Resources

Program Purpose and Accomplishments

Activity: Biotechnology Research (Public Health Service Act, Title III, Part A)

1974		1975		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
--	$11,559,000	Indefinite	--	$11,945,000

Purpose: The Biotechnology Research program awards grants and contracts for the development and use of sophisticated health-related technologies. Emphasis is placed on digital computation, mass spectroscopy, nuclear magnetic resonance spectroscopy, and electron microscopy, although other technologies also are included to a limited degree. The main thrust of this program is the furtherance of biomedical research through creation of centers of technological excellence which in turn provide the grantees and contractors of NIH's categorical programs with investigative opportunities they otherwise would not have. The biotechnology resource is characterized by four component activities: (a) the provision of technology and consultative services to biomedical scientists, especially those whose specific research projects are funded by the categorical Institutes of the NIH; (b) the conduct of collaborative research with members of the resource user community; (c) the pursuit of research and development directed toward upgrading existing resource capabilities and the state of the technology as it relates to human disease; and (d) the provision of a base for the training of biomedical scientists in the appreciation and use of technology.

Explanation: Applications for grant awards are submitted by institutions to the Biotechnology Research Program. Applications are reviewed by appropriate NIH Study Sections, program staff and the National Advisory Research Resources Council. Priorities of awards are determined by staff upon recommendations of the National Advisory Research Resources Council and are based upon the nature of the proposed research described in the application. The Biotechnology Research grants are project grants with no matching requirements. Resource awards are normally made for a period of from two to five years and are subject to renewal. In this program the contract mechanism is also used to support research with Federal and non-Federal agencies.

Accomplishments in 1974: The funds available in FY 1974 will provide for continued grant support to 55 biotechnology research resources and for biotechnology contract activities.

Objectives for 1975: In 1975 the funds requested will provide for continued support for 46 biotechnology research resources which includes payment for full indirect costs, and biotechnology contract activities.

NATIONAL INSTITUTES OF HEALTH

Research Resources

Program Purpose and Accomplishments

Activity: Laboratory Animal Sciences and Primate Research (Public Health Service Act, Title III, Part A)

1974			1975 Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
--	$17,916,000	Indefinite	--	$17,468,000

Purpose: The Laboratory Animal Sciences and Primate Research Program assists institutions in providing animal resources for biomedical research and provides special research environments where scientists can conduct biomedical and behavioral research using the nonhuman primate as the experimental animal. It also provides training grants and fellowship support in laboratory animal science and medicine to assure a continuing supply of research support personnel.

Project grants for Laboratory Animal Sciences are made to institutions for special animal colonies, research related to improving animal health and care, disease diagnosis and control, studies directed to enhancing the usefulness of animal models for research, improvement of institutional animal facilities and resources to meet requirements of the Animal Welfare Act of 1970, and institutional primate colonies.

Explanation: Applications for grant awards are submitted by institutions to the Laboratory Animal Sciences and Primate Research Program. Applications are reviewed by the Animal Resources Advisory Committee, the Primate Research Centers Advisory Committee, program staff, and the National Advisory Research Resources Council. Priorities of awards are determined by staff upon recommendations of the National Advisory Research Resources Council and are based upon the nature of the proposed research described in the application.

The Laboratory Animal Sciences and Primate Research Program grants are awarded in yearly increments for a project period up to five years and are eligible for renewal. There are no matching fund requirements in this Program. In addition the contract mechanism is used to support research with non-Federal agencies.

Accomplishments in 1974: The funds available in FY 1974 will provide for support of 86 animal resources and seven primate centers, 16 fellowship awards including implementation of the new postdoctoral research fellowships and training program in laboratory animal medicine and science; seven training programs and continued contract support for laboratory animal and primate research including the Holloman Air Force Base Chimpanzee Colony.

Objectives for 1975: The FY 1975 budget will provide for the support of 76 Laboratory Animal Science Projects and seven Primate Research Centers; four contract supported projects; 19 fellowships, and four training programs (about five trainees).

NATIONAL INSTITUTES OF HEALTH

Research Resources

Program Purpose and Accomplishments

Activity: General Research Support (Public Health Service Act, Title III, Part A)

1974			1975	
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
--	$45,250,000	Indefinite	--	0

Purpose: The General Research Support Grant Program was started in 1962 after the passage of Public Law 86-798. Within broadly defined guidelines, funds awarded to institutions engaged in health-related research may be spent for direct costs of health research in any way deemed appropriate by the recipient institution.

Explanation: Viewed as complementary to categorical project grants this grant program provided funds on a continuing basis to eligible institutions for their self determined flexible use in support of biomedical research and research training activities. The amount of each award is based on the total of the National Institutes of Health and the National Institutes of Mental Health research project grants received by each institution in the preceding fiscal year. Eligible institutions include schools of medicine, dentistry, osteopathy, public health and other types of health professional schools, hospitals, state and local health departments, non-academic health research organizations, and non-health related academic institutions.

Accomplishments in 1974: The funds available in FY 1974 will provide support to approximately 423 awardees.

Objectives for 1975: No funds are requested for this program in 1975 since the General Research Support Grant Program, which is designed to provide untargeted research funds to institutions to strengthen their biomedical research capacity, is of a lower priority than are program oriented research project activities. The NIH budget places a higher priority on maintaining financial and programmatic flexibility within the research project grant component of the NIH.

NATIONAL INSTITUTES OF HEALTH

Research Resources

Program Purpose and Accomplishments

Activity: Minority Biomedical Support (Public Health Service Act, Title III, Part A)

1974		1975		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
--	$7,000,000	Indefinite	--	$7,270,000

Purpose: The Minority Biomedical Support Program was designed to strengthen the institutional health-related research capabilities of four-year colleges, universities, and health professional schools in which student enrollments are drawn mainly from ethnic minority groups. It constitutes the major focus and concentrated effort of the NIH to involve minority institution scientists in biomedical research and to expose minority students to the challenges and opportunities in biomedicine.

Specifically, the Minority Biomedical Support Program will (1) enhance the biomedical research and training environment of minority institutions, (2) strenghten the facilities of minority institutions, (3) involve minority students in research, and (4) increase the number of minorities well-trained for health professional and graduate schools.

This program was initiated at the encouragement of the Senate Appropriations Committee, in order that members of minority groups may have equality of opportunity to become investigators in biomedical research.

Explanation: Applications for grant awards are submitted by institutions to the Minority Biomedical Support Program. Research applications are reviewed by the General Research Support Program Advisory Committee, program staff and the National Advisory Research Resources Council. Priorities of awards are determined by staff upon recommendation of the National Advisory Research Resources Council and are based upon the nature of the proposed research described in the application.

The Minority Biomedical Support Program grants normally are awarded for up to five years with funds provided in yearly increments. There are no matching fund requirements.

Accomplishments in 1974: In 1973, of the 38 institutions that received support in 1972, 36 received second year support based on prior commitments. Second year awards, reflecting increased program momentum, were made at higher levels than in the initial year. In addition, 15 other institutional components received awards, including one renewal and 14 new.

In FY 1974 the program was expected to include four-year colleges where there are large numbers of minority (i.e., Black, Spanish-speaking, American Indian, or Oriental) students, but not necessarily a majority (as required under previous MBS program guidelines). There are also a few junior colleges and community colleges where there are large numbers of minority students enrolled. By including these institutions and others such as the American Indian Tribal Councils, the program could reach a considerable number of minorities, including Spanish-speaking people and Indians, as well as many Blacks, who were originally excluded from the program. The desirability and feasibility of such changes in institutional eligibility is being closely followed. In 1974, the budget estimate will allow for continuing commitments to 51 institutions and approximately 8 new awards.

Objectives for 1975: The funds requested for FY 1975 will provide for support to 59 continuing awards and approximately eight new awards.

NATIONAL INSTITUTES OF HEALTH

Research Resources

Program Purpose and Accomplishments

Activity: Chemical Biological Information Handling Research (Public Health Service Act, Title III, Part A)

1974		1975		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
--	$1,000,000	Indefinite	--	$1,000,000

Purpose: The Chemical Biological Information Handling Research Program focuses on (a) designing and developing computer-based information-handling tools important to studies of chemical/biological interactions (a line of inquiry relevant to almost every major medical area); (b) making these tools available to the National scientific community in an easy-to-use and highly reliable form; and (c) collaborating with the users of these tools in order not only to refine and extend them, but also to develop deeper insights into the investigative process itself.

Explanation: Implementation of this program is largely through contracts with profit-making organizations, universities, and other Federal agencies.

Accomplishments in 1974: Fiscal year 1973 marked a major milestone in the evolution of the Chemical Biological Information Handling Research Program. During this year the PROPHET System--NIH's specialized computer resource for research on drugs and drug-related phenomena--emerged after over five years of intensive program-initiated design and development to become a service in support of the day-to-day information-handling requirements of more than 30 laboratory and clinical investigators at four remote terminal installations in three states. Moreover, as a result of a national competition conducted by the Program in 1973 to identify additional qualified PROPHET users, another ten sites (out of 28 applying)--with, conservatively estimated, up to 80 potential additional user-scientists have been identified and await access to PROPHET's services. By the end of 1974 it is planned that there will be six user sites and approximately 65 users.

Objectives for 1975: The funds requested in FY 1975 would be used for three objectives: (a) to enlarge the number of scientists using the PROPHET System; (b) to refine PROPHET's capabilities and operational efficiency; and (c) to undertake never-before-possible experiments in computer-mediated scientific communications involving the mechanisms of drug action.

NATIONAL INSTITUTES OF HEALTH

Research Resources

Program Purpose and Accomplishments

Activity: Research Management and Program Services (Public Health Service Act, Title III, Part A)

1974		1975		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
72	$2,486,000	Indefinite	72	$2,532,000

Purpose: This activity provides overall administrative management, scientific direction and coordination of the Division's programs.

Explanation: Funds are used for salaries and related cost for staff of the immediate Office of the Director, which includes administrative services, financial management, program planning; the Program Analysis Branch, and for staff necessary for program planning and development, and review and evaluation of grant and contract programs.

Accomplishments in 1974: During 1974 this activity continued to provide the overall direction and administration of the Division's programs, as well as review of current and proposed operations. For example, the establishment of more effective ways to properly allocate funds for the improvement of institutional animal resources so as to best meet the competing pressures of animal welfare and utilization of animals for biomedical research; the management of effective scientific and administrative linkages between existing biotechnology resources and general clinical research centers to more effectively exploit the technologies of physical sciences on behalf of the clinical research subject (the human patient); continuation of nonhuman primate breeding studies designed to help increase the supply of primates for biomedical research; and continued active participation in the search for qualified minority and female candidates for Federal employment and membership on advisory committees.

Objectives for 1975: In 1975, the Division will be involved in a number of activities designed to broaden and expand the impact of its programs. Among these are: (1) the continued evaluation of the Minority Biomedical Support Program to determine the feasibility of its expansion to include other institutions and organizations, such as two-year colleges, where a significant number of minority students are enrolled but where they do not constitute a majority of the student body; (2) further develop the research resource sharing concept to enable institutions which require sophisticated technology in order to conduct their research, but where the volume of research does not justify separate large and complex resources, to share existing resources of other DRR supported institutions; and (3) the development of new management and organizational concepts within the Division designed to more effectively serve the biomedical research community.

The funds requested in FY 1975 will provide continued support for this program including funds for the mandatory increases and within grade increases, postage and FTS rate increase, one extra day of pay and the NIH Management Fund for centrally furnished services.

FRIDAY, MARCH 29, 1974.

JOHN E. FOGARTY INTERNATIONAL CENTER FOR ADVANCED STUDY IN THE HEALTH SCIENCES

WITNESSES

DR. MILO D. LEAVITT, JR., DIRECTOR
DR. ROBERT S. STONE, DIRECTOR, NATIONAL INSTITUTES OF HEALTH
DR. DeWITT STETTEN, JR., DEPUTY DIRECTOR FOR SCIENCE, NATIONAL INSTITUTES OF HEALTH
GEORGE E. PRESSON, EXECUTIVE OFFICER, JOHN E. FOGARTY INTERNATIONAL CENTER FOR ADVANCED STUDY IN THE HEALTH SCIENCES
LEON M. SCHWARTZ, ASSOCIATE DIRECTOR FOR ADMINISTRATION, NATIONAL INSTITUTES OF HEALTH
LELAND B. MAY, ACTING DIRECTOR OF FINANCIAL MANAGEMENT, NATIONAL INSTITUTES OF HEALTH
CHARLES MILLER, DEPUTY ASSISTANT SECRETARY, BUDGET

Object Classification (in thousands of dollars)

Identification code 09-25-0819-0-1-651		1973 actual	1974 est.	1975 est.
	Direct obligations:			
	Personnel compensation:			
11.1	Permanent positions	952	979	1,008
11.3	Positions other than permanent	71	89	90
11.5	Other personnel compensation	11	16	16
	Total personnel compensation	1,034	1,084	1,114
12.1	Personnel benefits: Civilian	105	130	136
21.0	Travel and transportation of persons	127	140	140
22.0	Transportation of things	3	6	6
23.0	Rent, communications, and utilities	82	86	94
24.0	Printing and reproduction	36	50	100
25.0	Other services	843	1,061	1,369
26.0	Supplies and materials	87	88	95
31.0	Equipment	11	28	35
41.0	Grants, subsidies, and contributions	1,546	2,856	1,695
	Total direct obligations	3,874	5,529	4,784
	Reimbursable obligations:			
25.0	Other services	25	200	200
99.0	Total obligations	3,899	5,729	4,984

Personnel Summary

	1973 actual	1974 est.	1975 est.
Total number of permanent positions	55	49	49
Full-time equivalent of other positions	9	10	10
Average paid employment	62	59	59
Average GS grade	8.5	8.6	8.6
Average GS salary	$14,260	$15,138	$15,473
Average salary of ungraded positions	$11,138	$12,018	$12,253

Program and Financing (in thousands of dollars)

Identification code 09-25-0819-0-1-651		1973 actual	1974 est.	1975 est.
	Program by activities:			
	Direct program:			
	1. Gorgas Memorial Institute	500	500	500
	2. Scholars	446	2,356	1,195
	3. Research management and program services	1,858	2,673	3,089
	Total direct program	2,804	5,529	4,784
	Reimbursable program:			
	3. Research management and program services	25	200	200
	Total program costs, funded[1]	2,829	5,729	4,984
	Change in selected resources (undelivered orders)	1,070	---------	---------
10	Total obligations	3,899	5,729	4,984
	Financing:			
11	Receipts and reimbursements from: Federal funds	−25	−200	−200
25	Unobligated balance lapsing	792	---------	---------
	Unobligated balance restored	---------	−767	---------
	Budget authority	4,666	4,762	4,784
	Budget authority:			
40	Appropriation	4,666	4,767	4,784
41	Transferred to other accounts	---------	−22	---------
43	**Appropriation (adjusted)**	4,666	4,745	4,784
46.20	**Proposed transfer for civilian pay raises**	---------	17	---------
	Relation of obligations to outlays:			
71	Obligations incurred, net	3,874	5,529	4,784
72	Obligated balance, start of year	2,669	2,232	2,526
74	Obligated balance, end of year	−2,232	−2,526	−1,063
77	Adjustments in expired accounts	−58	---------	---------
90	Outlays, excluding pay raise supplemental	4,253	5,219	6,246
91.20	Outlays from civilian pay raise supplemental	---------	16	1

[1] Includes capital outlay as follows: 1973, $11 thousand; 1974, $28 thousand; 1975, $35 thousand.

Note.—Excludes $22 thousand in 1974 and 1975 for activities transferred to: Departmental Management, 1973, $22 thousand.

WITNESS INTRODUCTION

Mr. FLOOD. Now we have the John E. Fogarty International Center for Advanced Study in the Health Sciences. The presentation will be made by Dr. Milo D. Leavitt, Jr., the Director.

We have your biographical sketch, doctor, which we will place in the record.

[The biographical sketch follows:]

BIOGRAPHICAL SKETCH

Name: Milo David Leavitt, Jr;

Position: Director, John E. Fogarty International Center for Advanced Study in the Health Science, National Institutes of Health;

Date and place of birth: June 24, 1915, Beloit, Wis.;

Education: 1933–38, University of Wisconsin, bachelor of arts; 1938–40, University of Pennsylvania, doctor of medicine; 1945–48, University of Minnesota, M. Sci.; 1958–59, Harvard University, M.P.H.

Experience: 1968–present, Director, John E. Fogarty International Center for Advanced Study in the Health Sciences, National Institutes of Health; 1972–73, Member, U.S. delegation to 25th and 26th World Health Assemblies, Geneva; 1967–68, Acting Director, Office of Program Planning, National Institutes of Health; 1967, Deputy Director, Office of Program Planning, National Institutes of Health; 1966–67, Deputy Assistant Secretary for Science and Population, Department of Health, Education and Welfare; 1966, Science Policy Coordinator, OS–ASH, Department of Health, Education and Welfare; 1962–66, Head, Special International Programs Section, Office of International Research, National Institutes of Health; 1960–62, Assistant Chief, Perinatal Research Branch, National Institute of Neurological Diseases and Blindness, National Institutes of Health; 1959–60, Chief, Project Services Branch, Collaborative Research, National Institute of Neurological Diseases and Blindness, National Institutes of Health; 1958–59, Postdoctoral public health trainee, Harvard School of Public Health, Boston, Mass.; 1949–58, Clinical assistant professor of medicine, Medical College of Pennsylvania, Philadelphia, Pa.; 1945–49, Fellow, Internal Medicine, Mayo Clinic, Rochester, Minn.; 1942–45, Captain, U.S. Army Medical Corps; 1940–42, Rotating internship, Philadelphia General Hospital, Philadelphia, Pa.

Association memberships: American Medical Association, Philadelphia County Medical Society, Society of the Sigma Xi, American Diabetes Association, Association of American Medical Colleges, New York Academy of Sciences, American Association for the Advancement of Science, Industrial Medical Association, Alumni Association of the Mayo Foundation, American Public Health Association.

Mr. FLOOD. Who do you want us to know that you have with you?

Dr. LEAVITT. I am accompanied by my executive officer, Mr. George Presson.

Mr. FLOOD. You have a prepared statement. What do you want to do, Doctor?

Dr. LEAVITT. With your permission I would like to read it into the record.

Mr. FLOOD. Suppose you do.

OPENING STATEMENT

Dr. LEAVITT. Mr. Chairman and members of the committee, the Fogarty International Center, which was established by this committee to further the ideas and ideals of the late Congressman John E. Fogarty, expresses its mission as the effort to advance man's knowledge in the biomedical and related sciences through research, advanced study, and international cooperation and collaboration. The programs of the Center are designed to develop various aspects of this mission and provide an opportunity to examine major problems through a multidisciplinary approach.

If I may, I should like to address myself to some of those programs.

ADVANCED STUDY

The advanced study program of the Center provides opportunities for study and discussion of important research, public health, medical, social, and economic issues. It utilizes the skills and abilities of the National Institutes of Health and other Federal agency personnel, as well as outstanding scientists from the United States and abroad, and involves hundreds of individuals each year in its studies.

Last year, we discussed a number of areas of concern within this field of advanced study. Five of them—diseases of fetal and perinatal development, communicable diseases, derangements of dental health, diabetes, and obesity—have been completed and manuscripts are being readied for publication.

Studies on the remaining subjects—nutritional disorders, problems of population control, methods of disease detection, neurological and communication problems, diseases of the genitourinary tract, diseases of bones and joints, mental health problems, visual disturbances, and dermatologic disorders—were initiated during fiscal 1974. We expect that workshops, seminars, and conferences to discuss and elaborate upon these themes will be conducted during fiscal 1975, and publications of the proceedings will be made available in fiscal 1976.

The Center's cooperative program with the Association of Teachers of Preventive Medicine, which was designed to develop resource material for departments of preventive medicine, is well underway. Among the 12 topics considered, 7-study of academic relationships between preventive medicine and public health, health education, teaching resources for preventive medicine, chronic disease care primary care and family medicine, ancillary personnel, and consumer participation—have been the subject of workshop conferences. Proceedings of these workshops are in preparation. It is anticipated that these monographs will be published during fiscal 1975.

As a result of the Center's early attention to this broad field, we are pleased to note that the material developed by the various study groups has been utilized by the administration in developing program documents for its national health insurance program.

GEOGRAPHIC HEALTH STUDIES

Growing public interest in the health care of our citizens has encouraged the Center in recent years to examine the organization and administration of medical systems in other countries.

For example, studies of the medical system of the Soviet Union have provided us with a better knowledge of the legislative role of Government agencies, the health planning process, and biomedical research priorities in a planned economy.

Studies of the medical system in the People's Republic of China have also created for us an awareness of the importance of health as an instrument of public policy in a controlled economy which involves massive citizen participation, and the necessity of adapting the use of limited resources to treat the health problem of the world's largest population.

Another example, dealing with "National and Regional Health Planning in Sweden," examines this regional model as an approach to health services within a specific social order.

Although we may not wish to adopt any of these foreign medical systems in whole or in part, the knowledge gained permits a better understanding of health care which can be applied to our own problems.

FOGARTY SCHOLARS-IN-RESIDENCE

The Fogarty scholars-in-residence program has played an important role in the development of the Fogarty International Center as a center for advanced study in the health sciences by bringing distinguished scholars from various disciplines to the Center to pursue their scholarly interests and to contribute to the academic interests of the National Institutes of Health.

Their interests and contributions have ranged over broad scientific areas; in some cases, their impact and contributions have been direct and readily apparent. For instance:

Dr. Albert B. Sabin of the United States, who won world recognition for the development of an effective vaccine against poliomyelitis, has served as a Fogarty scholar during the past year. During his tenure as a scholar, Dr. Sabin has worked closely with the National Cancer Institute, devoting his major efforts to determine what role, if any, herpes viruses may play in the development of certain types of cancer in human beings. These important investigations are currently being expanded under Dr. Sabin's direction at the Frederick Cancer Research Center.

Dr. Margaret Mead, also from the United States, and probably one of the world's best known anthropologists, joined the program last September and became immediately involved in the conduct of seminars and conferences involving the National Institutes of Health and several of its component institutes. Dr. Mead's most outstanding contribution was in the form of lectures before scientific groups, calling attention to the grave ecological situation which now faces the entire world, threatening the quality of life, population, and environment. She has stated that the dangers of air pollution, for example, provide a basis for cooperation among countries, since artificial frontiers are quite useless under these circumstances. The problem of air pollution can be solved scientifically with international cooperation, though this opportunity may not last more than another 25 years. Dr. Mead expects to convene a conference on the atmosphere early in 1975 under the aegis of the Fogarty Center.

Dr. Michael Sela, a distinguished immunologist from the Weizmann Institute of Science in Israel, and presently a scholar-in-residence, is involved with National Institutes of Health colleagues in studies of protein structure and proper antigen design, that may lead to a better understanding of the immune response on a molecular and cellular level. These basic studies may potentially lead to the production of synthetic vaccines in the future and make unnecessary our present reliance upon toxins or attenuated viruses with which there is always some risk to the patient.

INTERNATIONAL COOPERATION AND COLLABORATION

Cooperation internationally has been a tradition of the United States. The late Congressman Fogarty, in an address in September 1963 before the Citizens Committee for the World Health Organization, espoused the idea of a center for research in biology and medicine "dedicated to international cooperation and collaboration in the interests of mankind * * *"

The Fogarty International Center has actively participated in cooperative efforts with international agencies, such as the Pan-American Health and the World Health Organizations. For example, a current problem in the United States is the development of physician assistant training programs. In view of the experience of many other countries in this area, the Fogarty International Center and the World Health Organization cosponsored a Conference on the Medical Assistant, which brought together experts from the United States and abroad to discuss and compare ongoing programs in their respective countries.

Mr. Flood. Is that what we call paramedics?

Dr. Leavitt. Yes, sir. In addition, representatives of 21 developing countries attended because of their interest in improving the availability and quality of primary health care services.

The proceedings of this Conference are being published in four languages.

In addition to these specific activities, the Center is responsible for the administrative support for the National Institutes of Health visiting program, the International Visitors Center, the special foreign currency program, the programing of foreign health professionals sponsored by the World Health and the Pan American Health Organizations, and the U.S. contribution to the Gorgas Memorial Laboratory.

For these programs and activities, the Fogarty International Center is requesting $4,784,000.

I shall be pleased to reply to any questions of the committee.

GORGAS MEMORIAL LABORATORY

Mr. Flood. Where is the Gorgas Memorial Laboratory located?

Dr. Leavitt. In Panama.

Mr. Flood. There is $500,000 in your budget for assistance to the Gorgas Memorial Laboratory.

Dr. Leavitt. Yes, sir.

Mr. Flood. How long have we been providing assistance to the Gorgas Memorial Laboratory?

Dr. Leavitt. Since its construction in 1929.

Mr. Flood. Not at great length, but for the record, while we have had it before, we should have a brief description of who was Gorgas, why it was named after Gorgas, why it is in Panama, and briefly what is this laboratory.

Dr. Leavitt. Yes, sir, I shall be very pleased to do that.

[The information follows:]

GORGAS MEMORIAL LABORATORY BACKGROUND

The Gorgas Memorial Laboratory, an instrument of the Gorgas Memorial Institute, located in Panama was incorporated in 1921 as a tribute to the unprecedented contributions of Major General William Crawford Gorgas to the health of Latin America and his role in eliminating health hazards during the construction of the Panama Canal. U.S. Government support for this laboratory began in 1929 with an appropriation of $50,000 to the Department of State for the maintenance and operation of the laboratory. In 1955 the responsibility for the Government contribution was transferred to the Public Health Service, specifically the National Institute of Allergy and Infectious Diseases. At that time, the contribution had risen to $250,000.

The John E. Fogarty International Center for Advanced Study in the Health Sciences was organized in July 1968 and the NIH in fiscal 1970 transferred the responsibility for the U.S. contribution to the Gorgas Memorial Laboratory from NIAID to the Center. Since 1965, the authorization for the contribution has been increased to $500,000 but the first appropriation at that level was in 1967.

The long range objective at Gorgas Memorial Laboratory of prevention and control is being carried out by the investigation of diseases that are important in the tropics, together with the various ecological factors influencing them. The need for broad scale ecological and epidemiological investigations are of increasing importance. In medical schools and related institutions there has been a reduction in the attention being given to the study and investigation of diseases of the tropics. However, the problems persist. Certain of these diseases are not only still present but are increasing throughout the warm climates, posing a potential threat to the United States. As one of a decreasing number of centers where research on these diseases is being pursued, Gorgas Memorial Laboratory is becoming more important.

Mr. FLOOD. You have $500,000 for the Gorgas Laboratory.

Dr. LEAVITT. The original U.S. contribution was for $50,000. I do not recall the precise date, Mr. Chairman.

Mr. Presson points out there was a request for $250,000. I would guess about 10 years ago. Then it has been $500,000 per annum for the last 6 to 8 years.

Mr. FLOOD. Provide for the record the amounts appropriated for the Gorgas Memorial Laboratory for each of the last 10 years.

Dr. LEAVITT. Yes, sir.

[The information follows:]

Amounts Appropriated for Gorgas Memorial Laboratory, 1965–74

1965	$350, 000	1970	500, 000
1966	350, 000	1971	500, 000
1967	500, 000	1972	500, 000
1968	500, 000	1973	500, 000
1969	500, 000	1974	500, 000

AUTHORIZING LEGISLATION

Mr. FLOOD. Also, for the record, cite the legislation which authorizes assistance to the Gorgas Memorial Laboratory, just the citation. You do not have to quote the legislation.

[The information follows:]

GORGAS MEMORIAL INSTITUTE LEGISLATIVE HISTORY

(*a*) Public Law 350.—70th Congress (H.R. 8128), May 7, 1928. An act to authorize a permanent annual appropriation of $50,000 to the Gorgas Memorial Institute of Tropical and Preventive Medicine for the maintenance and operation of the Gorgas Memorial Laboratory.

(*b*) Public Law 867.—80th Congress (S. 2341), July 1, 1948. An act to authorize an increase in the permanent annual appropriation to not to exceed $150,000.

(*c*) Public Law 339.—83d Congress (S. 1456), April 19, 1954. An act to amend the original act of May 7, 1928 (as amended), to authorize the Gorgas Memorial Institute to accept from any of the Latin American governments, or from any other sources funds for the use of the Gorgas Memorial Institute.

(*d*) Public Law 86–296.—86th Congress (S. 2219), September 21, 1959. An act to increase the annual appropriation authorization to not to exceed $250,000 and to appropriate, in addition, $250,000 for the construction and equipment of a new laboratory building.

(*e*) Public Law 86–617.—86th Congress (S. 3179), July 12, 1960. An act to authorize an increase to $500,000 for the construction of the new laboratory building.

(*f*) Public Law 89–181.—89th Congress (S. 511), September 11, 1965. An act to increase the authorization of appropriations for the support of the Gorgas Memorial Laboratory to not to exceed $500,000, effective fiscal years ending June 30, 1963.

Mr. FLOOD. By the way, is the $500,000 the full amount authorized?

Dr. LEAVITT. Yes, sir.

Mr. FLOOD. What is the total amount of the whole budget for the Gorgas Laboratory?

Dr. LEAVITT. In fiscal year 1973, the total funds were $1,921,455.

Mr. FLOOD. What other source of funds does the Laboratory have?

Dr. LEAVITT. The U.S. contribution was $500,000; interest and miscellaneous income was $2,741; research grants and contracts accounted for $1,418,714; bringing it to a total of $1,921,000.

Dr. STONE. Those are principally, but not exclusively, NIH grants and contracts. There is some support by the Army.

INTERNATIONAL FELLOWSHIPS

Mr. FLOOD. Your budget justifications indicate 73 fellowships to be supported in 1975 compared to 100 in 1974. How many fellowships were supported in fiscal years 1971, 1972, and 1973?

Dr. LEAVITT. We do not have the 1971, 1972, and 1973 figures available.

Mr. FLOOD. Provide it for the record.

[The information follows:]

Fogarty International Center—Fellowships Supported in fiscal year 1971–73

1971	136
1972	171
1973	100

Mr. FLOOD. Is this fellowship program being phased out?

Dr. LEAVITT. No, sir, it is not. It is operating at a reduced level, but it is not being phased out.

Mr. FLOOD. It is a sacred cow.

Why is the number of fellowships being cut back in 1975?

Dr. LEAVITT. We have had multiyear funding in 1974——

Mr. FLOOD. Why are the fellowships being cut back in 1975?

Dr. LEAVITT. Actually, we are increasing them to 73 in 1975, Mr. Chairman.

Mr. MILLER. You have to look at page 219. The new fellowships are increasing.

Mr. **Flood**. Take a look at page 219. Go down to the fellowships subtotal. 1974, 100. 1975, 73. I am not very good at mathematics, but 73 is less than 100, is it not?

Mr. **Miller**. Yes, sir.

Mr. **Flood**. Good.

Mr. **Presson**. In 1974, you will note there were 43 noncompeting continuations which were awarded out of money which was terminating as of the close of 1974. The new fellowships, the 57, includes 49 multiyear funding. So, it would mean as far as the new competitions are concerned, we are increasing in 1975 from 57 to 73.

Mr. **Flood**. Are these fellowships for only 1 year?

Mr. **Presson**. Normally they are, sir.

Mr. **Flood**. Can you renew them?

Mr. **Presson**. Yes, sir.

Mr. **Flood**. By the way, what do you pay these fellows?

Dr. **Leavitt**. Their award is $11,000 each per annum.

Mr. **Flood**. Again for the record, update your tables appearing on pages 1,111 to 1,114 of last year's hearings, showing the countries from which the fellowships come.

Dr. **Leavitt**. Yes, sir, we will be pleased to do so.

[The information follows:]

FOGARTY INTERNATIONAL CENTER - NATIONAL INSTITUTES OF HEALTH

INTERNATIONAL RESEARCH FELLOWSHIPS

Total Number - NEW Awards
FY 1958 - 1973

	FY 1958	FY 1959	FY 1960	FY 1961	FY 1962	FY 1963	FY 1964	FY 1965	FY 1966	FY 1967	FY 1968	FY 1969	FY 1970	FY 1971	FY 1972	FY 1973	GRAND TOTAL
TOTAL	17	50	68	92	107	101	106	107	102	92	95	96	74	79	113	37	1,336
Latin America	-	16	14	18	24	28	18	20	13	16	15	11	14	14	14	5	240
Argentina	-	2	2	2	1	4	3	1	3	2	4	2	3	3	1	1	34
Bolivia	-	-	-	-	-	-	1	-	-	-	-	-	-	-	-	-	1
Brazil	-	3	2	4	3	7	3	-	-	-	2	3	2	1	1	-	31
Chile	-	3	2	1	2	4	3	5	2	4	3	3	4	3	5	1	45
Colombia	-	1	1	2	4	1	2	2	-	-	1	1	1	-	1	-	17
Costa Rica	-	-	-	-	2	-	-	1	-	-	-	-	-	1	-	-	4
El Salvador	-	1	-	-	-	-	1	-	1	-	1	1	-	-	-	-	5
Mexico	-	2	3	3	3	3	1	3	4	6	3	-	3	4	5	2	45
Peru	-	2	3	3	4	6	2	4	2	1	-	-	-	-	1	-	28
Uruguay	-	2	1	3	2	2	1	3	1	3	1	1	-	1	-	1	22
Venezuela	-	-	-	-	2	1	1	1	-	-	-	-	1	1	-	-	7
West Indies	-	-	-	-	1	-	-	-	-	-	-	-	-	-	-	-	1
Europe	17	24	38	43	50	50	58	54	62	48	54	54	42	44	68	21	727
Austria	2	1	2	1	3	2	1	1	3	2	1	1	3	-	-	-	23
Belgium	1	2	2	4	2	2	3	1	3	3	5	4	5	4	5	2	48
Denmark	-	1	4	4	2	2	1	3	4	1	2	4	3	2	5	1	39
Finland	1	1	3	1	5	1	5	4	4	5	6	6	6	3	6	2	59
France	2	3	3	4	-	4	1	3	3	4	2	3	1	1	6	1	41
Germany	2	3	2	4	4	4	5	5	6	4	3	3	5	4	-	1	55
Greece	-	-	-	-	1	-	3	1	-	-	1	-	-	1	2	-	9
Ireland	-	-	1	-	3	1	-	4	2	2	2	3	-	3	-	1	22
Italy	1	2	2	4	5	5	6	4	6	3	6	6	4	4	5	-	63
Netherlands	1	2	3	1	2	1	4	1	4	1	3	1	2	2	1	1	30
Norway	2	2	3	2	3	4	5	5	6	6	4	5	1	4	8	1	61
Poland	-	-	-	-	3	3	5	6	4	3	2	-	-	3	2	2	33
Spain	-	1	3	4	3	6	3	1	2	3	4	3	4	4	6	2	49
Sweden	2	1	2	4	4	5	5	6	4	4	3	5	4	4	7	2	62
Switzerland	1	3	2	3	3	3	1	1	1	-	2	1	1	-	3	2	27
United Kingdom	2	2	3	5	3	5	5	6	5	6	5	5	3	3	7	2	67
Yugoslavia	-	-	3	2	4	2	5	2	5	1	3	4	-	2	5	1	39

	FY 1958	FY 1959	FY 1960	FY 1961	FY 1962	FY 1963	FY 1964	FY 1965	FY 1966	FY 1967	FY 1968	FY 1969	FY 1970	FY 1971	FY 1972	FY 1973	GRAND TOTAL
Africa	-	-	2	3	2	2	5	3	4	4	3	2	1	2	2	1	36
Nigeria	-	-	-	-	-	-	1	-	-	-	-	-	-	-	-	-	1
South Africa	-	-	2	3	2	2	4	3	4	4	3	2	1	2	2	1	35
Middle East	-	-	2	4	4	3	3	5	6	6	3	6	4	4	9	2	61
Israel	-	-	2	4	4	3	3	5	6	6	3	6	4	4	8	1	59
Lebanon	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1	1	2
So. Asia & Far East	-	10	12	24	27	18	22	25	17	18	20	23	13	15	20	8	272
Australia	-	2	2	3	5	3	5	5	4	4	5	5	3	4	5	1	56
Ceylon	-	-	-	1	-	-	-	-	-	-	-	-	-	-	-	-	1
India	-	-	-	3	2	-	2	2	3	2	3	3	3	3	1	1	28
Iran	-	-	2	4	4	-	1	-	-	-	2	-	-	-	-	-	13
Japan	-	2	3	4	4	7	5	6	6	4	4	6	4	2	6	2	65
Korea	-	-	-	-	-	-	-	-	-	-	1	2	-	-	1	1	5
New Zealand	-	2	-	3	4	2	4	5	1	5	4	2	1	4	5	2	44
Pakistan	-	-	-	-	1	-	-	-	-	-	-	-	-	-	-	-	1
Philippines	-	2	2	3	2	2	1	2	2	-	-	1	1	-	-	-	18
Taiwan	-	-	-	-	4	3	3	3	1	2	1	2	1	2	1	1	24
Thailand	-	2	3	3	1	1	1	2	-	1	-	2	-	-	1	-	17

FOGARTY INTERNATIONAL CENTER - NATIONAL INSTITUTES OF HEALTH

INTERNATIONAL RESEARCH FELLOWSHIPS

Total Number of Awards (New & Continuations)
FY 1958 - 1973

	FY 1958	FY 1959	FY 1960	FY 1961	FY 1962	FY 1963	FY 1964	FY 1965	FY 1966	FY 1967	FY 1968	FY 1969	FY 1970	FY 1971	FY 1972	FY 1973	GRAND TOTAL
TOTAL	17	52	69	92	115	172	184	167	166	176	154	173	137	130	163	85	2,052
Latin America	-	16	14	18	27	37	37	36	35	34	29	30	23	25	26	18	405
Argentina	-	2	2	2	1	5	3	4	7	3	7	5	5	7	3	3	59
Bolivia	-	-	-	-	-	-	1	-	-	-	-	-	-	-	-	-	1
Brazil	-	3	2	4	4	9	7	1	3	-	2	5	3	2	3	-	48
Chile	-	3	2	1	3	4	7	8	7	9	10	7	7	6	7	7	88
Colombia	-	1	1	2	4	3	6	4	1	1	1	2	2	-	1	1	30
Costa Rica	-	-	-	-	2	1	-	1	-	1	-	-	-	1	1	-	7
El Salvador	-	1	-	-	-	-	1	1	2	1	1	1	1	-	-	-	9
Mexico	-	2	3	3	3	4	2	5	4	10	6	5	4	6	10	5	72
Peru	-	2	3	3	4	7	7	8	7	3	1	-	-	-	1	-	46
Uruguay	-	2	1	3	3	3	2	3	3	5	1	5	-	2	-	2	35
Venezuela	-	-	-	-	2	1	1	1	1	1	-	-	1	1	-	-	9
West Indies	-	-	-	-	1	-	-	-	-	-	-	-	-	-	-	-	1
Europe	17	26	39	43	54	85	88	82	89	88	85	91	79	70	90	43	1,069
Austria	2	2	2	1	4	4	4	2	4	3	4	2	4	2	-	-	40
Belgium	1	2	2	4	2	8	3	5	4	6	8	5	8	8	5	4	75
Denmark	-	1	4	4	2	3	2	4	4	3	2	6	3	3	6	4	51
Finland	1	3	3	2	5	2	6	5	6	10	8	15	11	8	8	3	96
France	2	3	3	4	1	4	1	6	5	6	3	4	4	1	7	2	56
Germany	2	1	2	4	4	9	6	7	11	6	6	6	8	5	4	1	82
Greece	-	-	-	-	1	-	3	3	1	1	2	-	1	1	2	1	16
Ireland	-	-	1	-	3	1	1	4	3	5	3	5	1	3	1	2	33
Italy	1	2	2	4	5	8	10	8	8	7	9	8	12	7	5	1	97
Netherlands	1	2	3	1	2	2	4	1	4	4	5	1	2	2	2	1	37
Norway	2	2	3	2	3	7	10	7	9	7	4	8	3	4	10	2	83
Poland	-	-	-	-	3	2	6	7	4	5	5	3	-	3	2	4	44
Spain	-	1	3	4	3	9	5	5	6	5	4	7	9	5	12	5	83
Sweden	2	2	2	4	4	6	7	8	4	6	7	7	6	5	8	4	82
Switzerland	1	3	2	3	3	5	6	2	2	1	2	3	2	1	4	3	43
United Kingdom	2	2	4	5	4	7	7	6	5	8	7	6	3	8	8	5	87
Yugoslavia	-	-	3	1	5	8	7	2	9	5	6	5	2	4	6	1	64

	FY 1958	FY 1959	FY 1960	FY 1961	FY 1962	FY 1963	FY 1964	FY 1965	FY 1966	FY 1967	FY 1968	FY 1969	FY 1970	FY 1971	FY 1972	FY 1973	GRAND TOTAL
Africa	-	-	2	3	2	5	6	4	7	4	4	2	2	2	3	2	48
Nigeria	-	-	-	-	-	-	1	-	-	-	-	-	-	-	-	-	1
South Africa	-	-	2	3	2	5	5	4	7	4	4	2	2	2	3	2	47
Middle East	-	-	2	4	4	5	7	8	10	10	7	12	9	8	14	8	108
Israel	-	-	2	4	4	5	7	8	10	10	7	12	9	8	13	6	105
Lebanon	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1	2	3
So.Asia & Far East	-	10	12	24	28	40	46	37	25	40	29	38	24	25	30	14	422
Australia	-	2	2	3	5	5	12	5	4	9	8	7	7	5	6	3	83
Ceylon	-	-	-	1	-	-	-	-	-	-	-	-	-	-	-	-	1
India	-	-	-	3	3	3	5	3	3	4	4	4	5	4	3	2	46
Iran	-	-	2	4	4	4	3	-	-	-	2	1	-	-	-	-	20
Japan	-	2	3	4	4	12	10	7	8	13	7	10	7	8	10	2	107
Korea	-	-	-	-	-	-	-	-	-	-	1	3	1	-	1	1	7
New Zealand	-	2	-	3	4	3	4	6	4	6	4	5	1	5	6	4	57
Pakistan	-	-	-	-	1	1	-	-	-	-	-	-	-	-	-	-	2
Philippines	-	2	2	3	2	5	3	5	3	2	1	1	1	1	-	-	31
Taiwan	-	-	-	-	4	6	7	8	3	4	2	5	2	2	3	2	48
Thailand	-	2	3	3	1	1	2	3	-	2	-	2	-	-	1	-	20

MULTIYEAR FUNDING

Mr. Flood. How many fellowships were funded for 2 years in 1974?

Dr. Leavitt. Forty-nine.

Mr. Flood. Give us a breakdown of the dollars involved in that funding.

Dr. Leavitt. Yes, sir.

[The information follows:]

FOGARTY INTERNATIONAL CENTER

Obligations by Budget Mechanism Showing "True" Program Levels in 1974 - 1975 (Amounts in thousands)

	1972		1973		1974		1975	
	Number	Amount	Number	Amount	Number	Amount	Number	Amount
Grants								
Special								
Gorgas Memorial Institute..........	1	$ 500	1	$ 500	1	$ 500	1	$ 500
Fellowships								
Non-competing......................	50	396	51	407	43	427	49	544
New..................................	121	1,453	49	626	108	1,385	73	1,195
Supplemental.......................	(34)	28	(47)	13	---	---	---	---
Subtotal..........................	171	1,877	100	1,046	151	1,812	122	1,739
International Center.................	---	1,860	---	2,328	---	2,673	---	3,089
TOTAL..................................	172	4,237	101	3,874	152	4,985	123	5,328

Obligations by Budget Activity Showing "True" Program Levels in 1974 - 1975 (Amounts in thousands)

Budget Program	1973		1974		1975	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Gorgas Memorial Institute	---	$ 500	---	$ 500	---	$ 500
Scholars	---	1,046	---	1,812	---	1,739
Research Management and Program Services	55	2,328	49	2,673	49	3,089
Total	55	3,874	49	4,985	49	5,328

FOGARTY INTERNATIONAL CENTER

Multi-year Funding from
1974 Appropriation
(Amounts in thousands)

Budget Mechanism	No. of Awards	Total Amount	Amount Affecting 1975 Funding	Remarks
Research Grants..............	---	---	---	---
Fellowships..................	49	$1,088	$ 544	Scholars
Training Grants..............	---	---	---	---
Research & Development Contracts..................	---	---	---	---

Distribution of 1973
Impounded Funds
(Amounts in thousands)

Budget Mechanism	No. of Awards	Amount	Remarks
Research Grants...............	---	---	---
Fellowships...................	51	$ 571	Scholars
Training Grants...............	---	---	---
Research & Development Contracts...................	---	---	---
Other Direct Operations........	---	196	Research Management and Program Services
Total	51	767	

ADVANCED STUDIES

Mr. Flood. You want $596,000 for "new studies through contracts and conferences in the advanced and geographic health study areas." What do you have in mind there?

Dr. Leavitt. This $590,000 is for all of our advanced studies. This includes our support of conferences and bringing experts to Bethedsa to work with us. In fact, this supports a variety of activities under the advanced study program.

This would also include all of our contracts since we have no grants program and cannot make any grant award.

Mr. Flood. How many conferences will you hold in 1974 and on what subjects?

Dr. Leavitt. We will be very pleased to provide that for the record. We have held about 15 thus far in 1974 with an approximate total of 25 for the year.

Mr. Flood. What were some of the subjects?

Dr. Leavitt. I will provide that.

Mr. Flood. From one extreme to the other, give me two or three.

Dr. Leavitt. Primary care and preventive medicine is one.

Diseases of the liver and the biliary tract. This was a conference at which we worked on nomenclature and diagnostic criteria and diagnostic methodology in liver disease.

Another one was vasoactive peptides in hypertension, a basic science subject.

Mr. Flood. What is the most exotic one you have there?

Dr. Leavitt. We are going to work with the Dental Institute in determining how the desire for sweetness develops in the human infant, the genesis of preference for sweet taste.

Mr. Flood. Everybody says a baby is sweet.

Dr. Leavitt. This has to do with taste perception and why we like sweets, why some people like sweets more than others. This may have implications for the development of obesity in babies and in the maturing individual.

CONFERENCE SUPPORT

Mr. Flood. How much will each one of those conferences cost?

Dr. Leavitt. The cost varies from $15,000 to $25,000.

Mr. Flood. Is that a lot?

Dr. Leavitt. That is about average, Mr. Chairman. This includes the travel of participants, not only from the United States, but from abroad, and a modest subsidy for their stay.

Mr. Flood. What do the costs entail?

[The information follows:]

Elements of Conference Costs

Travel, per diem, audiovisual support, including transcription and printing.

Mr. Flood. How many conferences do you expect to hold in 1975 and how much do you expect each one of those to cost?

Dr. Leavitt. We would have to make an estimate on that.

Mr. Flood. Surely.

Dr. Leavitt. I would think that the cost——

Mr. Flood. How many are you going to hold?

Dr. **Leavitt**. Twenty-five. On the average, we conduct 25 conferences per year. The cost there might increase modestly because of transportation costs.

Mr. **Flood**. What will some of those subjects be?

Dr. **Leavitt**. As I point out in my opening statement, we are going to continue our studies of genitourinary disease, our work with the Association of Teachers of Preventive Medicine, getting information which has been developed from our conferences out to medical schools, schools of public health, and to the public.

Dr. **Stone**. Would it be helpful to you, Mr. Chairman, to know something about how the subjects are selected?

Mr. **Flood**. Yes.

Dr. **Stone**. We might cover that, then.

Mr. **Flood**. Who and how.

Dr. **Stone**. Yes, sir.

Mr. **Flood**. Does somebody get a brainstorm, literally or figuratively, or is this really a constructive program?

[The information follows:]

The Fogarty International Center has developed a conference program philosophy which emphasizes the sponsoring of meetings on subjects of broad, interdisciplinary interest within the international biomedical community. The major conceptual themes which form the basis of conference activity originating within the Fogarty International Center include the following:

I. Preventive medicine and health care delivery.
II. Environmental health.
III. Medical education.
IV. International health research and education.
V. Societal factors influencing health and disease.
VI. Advanced topics in biomedical research.

In addition proposals for total or partial support of conferences are received from other agencies within the Department as well as from university health science departments throughout the United States. Finally programs may be developed in collaboration with international and national health organizations as well as private foundations dedicated to human health. During the past 2 years preference has been given to subjects which relate to the six major themes. Accordingly great attention has been paid to the preventive medicine categorical state of the art reviews, preparation of resource material for the teaching of preventive medicine, and coordination of preventive-medicine philosophy within the Department.

Selection of topics is based on information derived from a variety of sources including the National Institutes of Health and other agencies within the Department, planning and editorial committees selected from Department and university and other public and private sector resources and specific solicited and unsolicited proposals. In all cases, scientific quality, pertinence to Fogarty International Center programs, and relative subject priority is determined by internal and external review mechanisms. As a result of this general philosophy of theme selection and subject review, we attempt to create a constructive program dealing with major issues of human health.

CONTRACTURAL SERVICES

Mr. **Flood**. For what purpose do you use contracts?

Dr. **Leavitt**. Our greatest use is the personal services contracts, by which we bring Professor X and Dr. Y from the University of Pittsburgh or the University of London to confer with us for 2 or 3 days.

Mr. **Flood**. Why do you want an increase of $330,000 for contracts in fiscal year 1975?

Dr. LEAVITT. This is for the conferences that we plan to hold in 1975.

LIST OF CONFERENCES

Mr. FLOOD. Will you give us a list of the conferences in 1974, the number of participants in each, and the dollar amount involved?

[The information follows:]

CONFERENCES SPONSORED BY THE FOGARTY INTERNATIONAL CENTER

	Participants		
Conference	Domestic	Foreign	Cost
Preventive medicine and health care delivery:			
Prevention of human health problems:			
Prevention of derangements of dental health	14	3	$6,957
Prevention of embryonic, fetal, and perinatal disease	35	6	9,544
Prevention of obesity	95	9	33,207
Educational aspects of preventive medicine (ATPM series):			
Role of social and behavioral sciences in preventive medicine	12	1	2,908
Academic relationships between preventive medicine and public health	33		5,982
Role of U.S. biomedical institutions in international health programs	27		3,351
Health education and communication for public health	13		15,378
Teaching resources in preventive medicine	31		5,430
Teaching of chronic illness and aging	38		7,470
Primary care in family medicine	10		1,958
Ancillary personnel in preventive medicine	50	6	21,808
Consumer participation in preventive medicine	30	9	14,042
Measurement of outcome in children with chronic illness	25		3,000
International health research and education:			
The medical assistant: WHO/FIC: Intermediate levels of health-care personnel	32	25	38,403
Advanced topics in medical research:			
Clinical research:			
WHO/DDH international collaborative study of dental manpower systems in relation to oral health status	10	12	12,769
Pharmacology and pharmacokinetics: Problems and perspectives	39	11	15,245
Role of neural crest in normal and abnormal embryogenesis	30	12	9,162
Pneumocystis carinii pneumonia	25	5	17,626
Standardization of nomenclature, diagnostic criteria, and diagnostic methodology for diseases of the liver and biliary tract	44	26	32,000
Intraoperative protection of the myocardium	15	6	9,000
Development of upper respiratory form and function—Implications for SIDS	38	2	15,000
Heart arrhythmias	20	6	6,000
Basic research:			
Genetic control of mutation	26	12	14,599
Regulation of gene expression in mammalian cells	44	9	17,532
Poly ADP-ribose	36	13	13,227

FELLOWSHIPS

Mr. FLOOD. Also, give us a table showing the number and, of course, always the dollar amounts, for fellowships for fiscal years 1972, 1973, 1974, and 1975, breaking that down into new awards and continuation awards.

[The information follows:]

FOGARTY INTERNATIONAL CENTER—FELLOWSHIPS

[Amounts in thousands]

	1971 obligations		1972 obligations		1973 obligations		1974 estimate		1975 estimate	
	Number	Amount	Number	Amount	Number	Amount	Number	Amount	Number	Amount
Noncompeting continuations	51	$301	50	$396	51	$407	43	$427		
New	85	935	121	1,435	49	626	108	1,929	73	$1,195
Supplemental	(32)	10	(34)	28	(47)	13				
Total	136	1,246	171	1,877	100	1,046	151	2,356	73	1,195

SYNTHETIC VACCINES

Mr. FLOOD. In your opening statement you talked about the work of Dr. Michael Sela which may lead to the production of artificial vaccines. Very interesting. What is an artificial vaccine vis-a-vis a vaccine?

Dr. LEAVITT. The antigen, the substance that causes the disease or infection, is a protein, a very complex protein. Dr. Sela has been able by working on protein at the molecular level——

Mr. FLOOD. Causes what disease?

Dr. LEAVITT. A variety of bacterial or viral agents. Sometimes we take an antigen and attenuate it. We may mix it with formaldehyde, for example, so it does not cause a specific disease but instead causes an immune response in the patients receiving it.

Sometimes, as we learned in the polio experience, the polio virus persisted live and created poliomyelitis among some of the people receiving it.

If Dr. Sela's work proves out, as we hope it will, we will be able to create a synthetic vaccine using certain kinds of proteins that will not induce disease but will induce or cause the human body to react as though a natural antigen has been employed. It will then give protection against the disease.

Mr. FLOOD. It is an entirely new philosophy of vaccine?

Dr. LEAVITT. It is a significant development. It is really an innovative and new approach.

Mr. FLOOD. Do we use any such things now, experimentally or on the market, or both?

Dr. LEAVITT. No, sir. This maybe a forerunner of things to come. That is why I thought it important to bring it to the committee's attention.

Mr. FLOOD. Yes. I do not want to take the time now, but suppose for the record you develop that a little bit. That is a very exciting statement. Indicate the potential, if there is such, for storage, deterioration, and so on, what elements are important to the whole spectrum of vaccines, and how an artificial vaccine will affect the various elements in that spectrum.

[The information follows:]

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MEDICAL WORLD NEWS February 22, 1974

The vaccine vanguard: synthetics

Vaccines of the future, whether viral or bacterial, may be constructed by the chemist rather than, as today, cultivated by the biologist. Immunization with such synthetic antigen molecules is already being done experimentally in sheep and goats.

"There is no reason why, once the molecular structure of the antigenically active part of a virus or a bacterium is known, it is not possible to prepare it in the test tube," maintains Dr. Michael Sela, chairman of chemical immunology at the Chaim Weizmann Institute in Rehovot, Israel. Dr. Sela outlined this concept at the Gustav Stern symposium on basic virology in New York (see p. 12). He is spending a year in the U.S. as a Fogarty scholar at the National Institutes of Health.

The advantages of biologically active synthetic materials over natural antigens for immunization include:

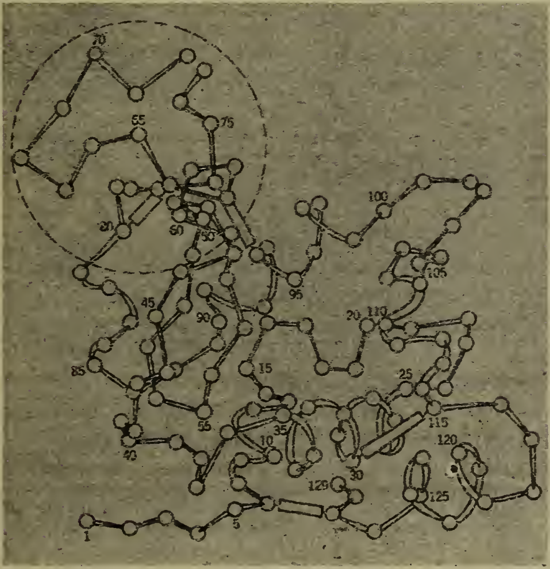
- Greater purity, since only the immunologically active part of the protein is actually injected;
- Ease of manufacture, because many significant disease-causing organisms are difficult—perhaps impossible—to cultivate in the laboratory for vaccine production. But once the structure of the immunologically active part of the pathogen is determined it can be synthesized;
- Improvement in response, since altering the structure of the antigen enhances its immunologic potential;
- Multivalent combinations are possible, since with a number of different antigenic molecules on hand it would be possible to prepare vaccines to protect against a number of different diseases with a single dose. "Because of antigenic competition, there is an upper limit, of course, to the number of different antigens that can be included within a single molecule," Dr. Sela points out. "But when one remembers that today there are some 26 different vaccines, and that we may end up with 30 or 40 vaccines, then the advantages of cutting the number of agents is clear."
- Chemical vaccines can be individually tailored to achieve maximum response. Most interesting, in Dr. Sela's view, is the possibility of tailoring synthetic agents to an individual's ability to respond to the antigen.

The basis for Dr. Sela's prediction about future vaccines is the fact that only small parts of an antigenic protein play a role in stimulating antibodies. Using lysozyme, a protein present in egg white, Dr. Sela and his associate, Dr. Ruth Arnon, succeeded in excising a small portion of the molecule—a loop containing a sequence of only 24 amino acids out of the total of 129 that make up the entire molecule. Attaching this loop to a synthetic polymer, they injected it into rabbits and goats and found that it elicited antibodies that reacted with whole natural lysozyme. When they immunized animals with this molecule—attached to a synthetic carrier—it gave antibodies similar in every respect to those they obtained with the natural loop.

"Conceptually, the road to synthetic immunization is now open," Dr. Sela says. "Of course we don't know enough yet about the coat protein of, say, poliovirus or of the other pathologically significant viruses to do the same as we've done with lysozyme," he adds, "but our knowledge of protein chemistry is advancing rapidly."

But he concludes on a note of caution: Immunization by synthetic antigens, while technically feasible, is unlikely to be done on any large scale for some time. The antigenically active sites of the major pathogenic viruses and bacteria have still not been isolated, much less synthesized, and so far there have been no studies on the persistence of antibodies stimulated by synthetic vaccines. Finally, he says, it is not certain that this approach will be successful for all pathogenically significant viruses. ■

Inside the circle is the antigenically active loop of lysozyme molecule that has already been synthesized: does it foreshadow a new vaccine era?



Mr. Flood. Mr. Robinson.

Mr. Robinson. Thank you, Mr. Chairman.

DECREASE IN FELLOWSHIP SUPPORT

I would like to explore a little further the matter the chairman went into with you regarding the decrease in fellowships. On page 211 of your justification, under "Decreases", under paragraph B, "Program," you say: "The decrease of $590,000 will result in a decrease of awards to scholars. The additional decrease of $571,000 representing restored funds will result in a decrease of awards to scholars."

What is the net effect of those two sentences if it does not indeed decrease the number of fellowships that are available at the present time?

Mr. Presson. The $590,000 is the decrease in fellowships between the 1974 money and the 1975 money. The $571,000 is the impounded funds restored in 1974 and must carry forward to 1975. This is why you have the two separate sums spoken to in the justification.

Mr. Robinson. The two need to be added together to represent the total?

Mr. Presson. Yes, sir.

Mr. Robinson. So, there is over $1 million less in terms of money, and if the $571,000 were not carried forward, the $590,000 would be a decrease?

Mr. Presson. That is correct.

Mr. Robinson. So from the standpoint of the total program, there will be over $1 million?

Mr. Presson. That is correct, sir.

INTERNATIONAL AIR POLLUTION

Mr. Robinson. You mentioned Dr. Margaret Mead and her interest and contributions in the area of international air pollution. We know, of course, that the Environmental Protection Agency is also involved in the area of international air pollution; and the international organization, I think, has an appropriation of between $8 and $9 million that goes to this area of research right now.

I wondered to what extent there is cooperation between the Center and the Environmental Protection Agency and these other areas that are interested in international air pollution.

Dr. Leavitt. On an informal basis, we did make arrangements for Dr. Mead to meet with other agencies, including the Environmental Protection Agency, during her stay at the Center. She did a most effective job of calling attention to some of these problems and pointing out the need for our all working together instead of separately.

Dr. Stone. The conference will certainly represent an integrated effort with regard to functional relationships.

I might suggest that when Dr. Rall from the Institute of Environmental Health Sciences testifies, we could pursue this further. He could describe some of the functional interrelationships between the various agencies concerned with similar problems.

Mr. Robinson. Under the sponsorship of the United Nations, we, the United States, fund a program in which we participate to the extent of about 40 percent in terms of worldwide activities in the area of air pollution. It would certainly seem important that coordination be properly accomplished with regard to your interest in the Center.

FOREIGN MEDICAL CARE SYSTEMS

With respect to the statement that the Center serves as a focal point for international activities of the National Institutes of Health, and your further statement on page 4 that "We may not wish to adopt any of these foreign medical systems in whole or in part" that have been researched as a result of this international interest, what about some of the systems that we might want to adopt? Are there foreign medical systems that are better than ours that we should consider adopting today, that have been discovered through this international interest?

Dr. LEAVITT. Yes, sir. I do not think there is any one system that we would wish to adopt. I think there are some aspects of the British national health system that would be applicable to the United States. There are other parts, as my British friends point out, that we would not want any part of because, from their experience, they have not been very successful.

I think we should make the most of what we can learn from somebody else's mistakes so that we do not make them in the United States. We have not completed our full study of other health systems. We have touched upon the Soviet and the Chinese health systems. We will soon have a volume devoted to the Swedish health system. We would like to profit by others' mistakes and use only those aspects that are really worthwhile.

Mr. ROBINSON. I certainly agree with you.

NATIONAL HEALTH INSURANCE

You say that "we are pleased to note that the material developed by the various study groups" at the center "has been utilized by the administration in developing program documents for its national health insurance program."

I wonder if, for the record, you would cite the instances of what those program documents are.

Dr. LEAVITT. Yes, sir, I would be pleased to do that.

[The information follows:]

The Fogarty International Center has attempted to assist with the assembly of background information in the development of department policy regarding the potential and relative priority of preventive medicine concepts and preventive services practice in providing comprehensive health care in the United States. Toward this end the Fogarty International Center has convened several meetings of experts in the field, prepared working background documents and attempted to coordinate contributions from experts in the private and public sectors as well as from within the Department. The final published expression of this effort will be a document entitled "a strategy for prevention" containing information presented in the attached outline. To date, part III., summary of preventive services, has been submited in support of preventive services proposals for the administration plan for comprehensive health insurance.

PROPOSED FORMAT FOR PREVENTIVE MEDICINE REPORT
A STRATEGY FOR PREVENTION

I. Introduction:
  Magnitude of the problem
  Morbidity, mortality
  Role and expectations of prevention
II. State of the art review (categorical):
  Program summaries-current
  Expression of life/cost savings
  Estimates of cost
  Financing mechanisms
  Delivery: relationship to sick-care
III. Summary of preventive services: Preventive services packages
IV. Organizational concepts:
  Surveillance of disease and health
  Performance standards
  Control/monitoring
  Financing requirements
V. Public health control:
  Environmental aspects of health maintenance
VI. Economic impact of preventive services:
VII. Resources required:
  Research, field studies, fiscal, manpower:
  To further the state of the art

Mr. ROBINSON. That is all, thank you, Mr. Chairman.

Mr. SMITH. No questions.

EXAMPLES OF FOGARTY SCHOLARS

Mr. CONTE. Could you give us some examples of the kinds of scientists who have been Fogarty Scholars and the problems they've worked on at the center? For the record, please.

[The information follows:]

Dr. Albert Sabin, the eminent virologist who is world renowned for his work on the live polio vaccine, spent the entire year 1973 as a Fogarty Scholar. His interests for the most part were oriented toward the cancer problem and shortly after his arrival he spent several weeks in the laboratory confirming some of his earlier findings. Shortly thereafter he reported through the scientific journals his work confirming earlier suspicions that there was a relationship between the herpes simplex virus and nine specific cancer sites, that is, lip, mouth, oropharynx, nasopharynx, kidney, bladder, prostate, cervix, and vulva. Dr. Sabin's involvement as a Fogarty Scholar resulted in his having a close relationship with the staff of the National Cancer Institute which ultimately led to his being offered a senior consultantship with immediate involvement in program planning of the Viral Oncology Unit of the Institute.

Prof. Torsten Teorell. During one of his earlier periods in residence, Professor Teorell organized a rather large international conference in the field of pharmacokinetics. His expertise related more to membrane permeability, which is a crucial point when one studies the effects of drugs in a biological system. The total drug problem has commanded considerable interest in this Nation, in fact worldwide, and the very timely conference in pharmacokinetics was well attended and shed considerable light on many of the basic problems involved.

Also, Professor Teorell, during a prior period of tenure, organized an international conference on normal and abnormal heart rhythmicity. As a biophysicist and physician, Professor Teorell has for a long time been extremely interested in sudden death. His interests relate primarily to the electrical and mechanical stimulation of the heart and he is interested in answering the problem "Why does this happen?" In cooperation with the National Heart and Lung

Institute, he organized a very meaningful conference which brought together clinicians as well as basic scientists to discuss the total problem.

During the last week of April, Professor Teorell once again is spearheading a conference involving the heart and lung and the subject of his conference will relate to cardiac arrhythmias. In each of the above instances, a Fogarty Scholar has quite successfully taken the initiative in a program area and brought together a number of scientists who might otherwise not have the opportunity to discuss their viewpoints on the problems involved.

Prof. P. C. C. Garnham, distinguished parasitologist and world expert in the field of malaria, undertook limited laboratory research in the National Institute of Allergy and Infectious Diseases, related closely to scientific staff and presented a number of lectures while here. In addition, he visited many academic institutions and primate centers where he presented lectures and was involved in seminars. Personal relationship to colleagues provided a tremendous stimulation to young scientists at NIH in the broad field of protozoology.

Prof. John T. Edsall, a distinguished physicist biochemist of Harvard University, in cooperation with a former colleague, Prof. Jeffries Wyman, a physiologist of the Regina Elena Institute in Rome, Italy, conducted a sophisticated seminar series on allosteric interactions. This proved to be an extremely informative type of presentation to a number of senior scientific staff both at the NIH and in the entire Washington area. These studies are fundamental to a number of disease processes particularly in the field of blood disorders.

Prof. Ragnar A. Granit, distinguished scientist, Nobel Laureate, and former president of the Nobel Institute of Neurophysiology, Karolinska Institute, is a recognized authority on the physiology of movement. His presence was most advantageous to the staff of the National Institute of Neurological Diseases and Stroke, whose interests focused on diseases involving neurological disorders in relation to muscular activity. Professor Granit, through personal consultation and involvement in seminars, was able to transmit a number of ideas and overall stimulation to the scientific community. One of his most significant activities was the conduct of an international conference at the Center devoted to "The control of movement and posture."

Prof. Ronald Christie, former dean of the Medical School at McGill University, Canada, while a Fogarty Scholar worked on a document to be published very shortly which involves an in-depth study of the comparative medical curricula of a number of countries throughout the world, including a breakdown by selected States within the United States. Dr. Christie's principal interest while here was in medical education and he conferred frequently with staff of the NIH Bureau of Health Manpower.

Prof. Charles S. Davidson of the Department of Clinical Medicine, Harvard Medical School, and an expert in liver disease, related primarily to the staff of the Clinical Center during his tenure as a Fogarty Scholar. His major contribution was the development of an improved program plan for the training of young clinical research associates at NIH. At the same time, Dr. Davidson participated actively in the clinical study of liver disease.

SELECTION OF SCHOLARS

Mr. CONTE. Do you select scholars for any one year to focus in a specific area, or do you try to cover a broad range of interests?

Dr. LEAVITT. Although we have scholars representing a broad range of interests, from time to time we have purposely invited combinations of scholars whose interests have focused in a specific area.

During the fall of 1972, Dr. Ronald Christie of McGill University and Sir Sydney Sunderland of Melbourne, Australia were brought here as scholars. Each has been dean of a medical school. Their common experience and interest led to cooperation in the field of medical education.

On another occasion, Dr. John T. Edsall of Harvard University and Dr. Jeffries Wyman from the Regina Elena Institute in Rome, Italy, were brought together to cooperate in the study of allosteric interactions.

During the coming summer, we shall have a grouping of four scholars around the broad area of immunology and protein chemistry. At the moment it is a very active field and with Professor Michael Sela of the Weizmann Institute of Israel, Professor Elvin Kabat of Columbia University, Professor Osamu Hayaishi of Kyoto University in Japan, and Professors Lars Ernster of the University of Stockholm, we anticipate a very active and concerted effort in the broad area of immunology.

FELLOWSHIPS

Mr. CONTE. Are you planning to award any new international fellowships from 1975 funds?

Dr. LEAVITT. Yes, 62.

DISSEMINATION ACTIVITIES

Mr. CONTE. How do you make material from your seminars and workshops more widely available?

Dr. LEAVITT. We believe it is our obligation to provide the proceedings of Fogarty conferences and workshops to scientists who do not attend our meetings because of space limitations. To this end, we have issued publications based on about 70 percent of our conferences. The methods of publication and distribution are suited to the nature of the meeting and the audience to whom they are directed. For example, conference summaries have been published in scientific journals or as pamphlets which have been distributed through appropriate mailing lists. Full conference proceedings have been published in journals, through special interest commercial pulishers, and as hardbound books in the Fogarty Center Proceedings Series. Thus, subscribers to journals, including individuals and libraries, receive our conference proceedings; books are distributed by commercial publishers to the scientific community; and the Fogarty Center Proceedings Series is distributed through appropriate mailing lists to individuals and to United States and foreign medical libraries. Of course, all books published by the Government Printing Office are available at low cost upon request.

YOUNGER SCIENTISTS

Mr. CONTE. Do you have any special programs for younger scientists or potential scientists?

Dr. LEAVITT. There is no special program for younger scientists at the present time; however, the International Research Fellowship is open to young, promising foreign biomedical scientists who have earned a doctoral degree in the sciences, or a professional degree in medicine, dentistry or veterinary sciences. Therefore, the range of applicants will include the very young physician, dentist, veterinarian or biomedical scientist who has considerable research experience, but who is still in the developmental stage in his career.

We purposely invite young scientists and physicians for conferences in subjects such as medical and graduate curriculum reform or the roles of paramedical personnel in health care delivery, since their views are essential in discussing these topics. For conferences in research topics, younger scientists are frequently the individuals who are performing the research and they are invited to present their work to the conference participants. Many of our meetings are open to NIH scientists who attend as space permits.

During the past 2 years we have encouraged Fogarty scholars-in-residence to conduct informal scientific sessions at Stone House with the expressed intent of involving young scientists who might otherwise not have an opportunity to contact the scholars. We have had a number of these meetings and they have worked very successfully and we feel to the advantage of all concerned. Though we have not labeled it a program as such for younger scientists, we plan to continue this policy and on the average we have one meeting scheduled each month. The more recent sessions have been in the field of immunology and liver diseases reflecting the interests of the current scholars-in-residence.

Mr. CONTE. Do you ever arrange for advanced students to sit in on seminars or conferences?

Dr. LEAVITT. Advanced students attend our meetings occasionally, but we have not made an effort to include persons below the Ph.D. or M.D. level in our conferences.

Mr. FLOOD. Thank you very much, gentlemen.

NATIONAL INSTITUTES OF HEALTH

John E. Fogarty International Center for Advanced Study in the Health Sciences

Amounts Available for Obligation [1/]

	1974 Revised	1975
Appropriation	$4,767,000	$4,784,000
Proposed supplemental*	17,000	---
Subtotal, adjusted appropriation	4,784,000	4,784,000
Real transfer to:		
"Departmental management" (For Department-wide reductions in public affairs)	-22,000	---
Subtotal, budget authority (base obligations)	4,762,000	4,784,000
Unobligated balance - restored	767,000	---
Total, obligations	5,529,000	4,784,000

[1/] Excludes the following amounts for reimbursable activities carried out by this account: 1974-$200,000; 1975-$200,000.

*Pay transfer

Summary of Changes

1974 Estimated obligations	$5,529,000
1975 Estimated obligations	4,784,000
Net change	-745,000

	1974		Change from 1974	
	Pos.	Amount	Pos.	Amount
Increases:				
A. Built-in				
1. Within-grade pay increases	---	---	---	$16,000
2. Extra day of pay	---	---	---	4,000
3. Bureau of Employment Compensation rate increase	---	---	---	2,000
4. Service and supply rate increase	---	---	---	2,000
5. Annualization of pay increases	---	---	---	14,000
				38,000
B. Program				
1. International Center	49	$2,430,000	---	596,000
Total, increases	---	---	---	634,000
Decreases:				
A. Built-in				
1. Payment to NIH Management Fund	---	---	---	-22,000
B. Program				
1. Fellowships	---	2,356,000	---	-1,161,000
2. International Center	49	2,430,000	---	-196,000
Total, decreases	---	---	---	-1,379,000
Total, net change	---	---	---	-745,000

Explanation of Changes

Increases:

A. Built-in--The increases will provide: $16,000 for within-grade pay increases, $4,000 for an extra day of pay, $2,000 for rate increases of the Bureau of Employment Compensation, $2,000 for service and supply rate increases, and $14,000 for annualization of the 1974 pay increase.

B. Program--The increase of $596,000 will permit increased activities within the advanced study area, with increased effort in preventive medicine studies and geographic health studies.

Decreases:

A. Built-in--Payment to NIH Management Fund--The decrease of $22,000 is for reduced assessments for centrally furnished services, such as patient care, receipt and initial review of all grant applications, computer services, maintenance of buildings and grounds, custodial services, communications, and transportation.

B. Program--

1. Fellowships--The decrease of $590,000 will result in a decrease of awards to scholars. The additional decrease of $571,000 representing restored funds will result in a decrease of awards to scholars.

2. International Center--The decrease of $196,000 representing restored funds will result in reduced program support in the International Center.

Obligations by Activity

Page Ref.		1974 Base*		1975 Estimate		Increase or Decrease	
		Pos.	Amount	Pos.	Amount	Pos.	Amount
	Grants:						
220	Gorgas Memorial Institute..	---	$500,000	---	$500,000	---	
221	Scholars..................	---	1,785,000 (2,356,000)	---	1,195,000	---	-590,000A
222	Research management and program services...........	49	2,477,000 (2,673,000)	49	3,089,000	---	+612,000B
	Total, obligations (base)....	49	4,762,000	49	4,784,000	---	+22,000
	Total, obligations...........		(5,529,000)				

Explanation of Changes

A) Funding a portion of the 1974 scholarship program on a two year basis will permit a decrease of $590,000 in the 1975 estimate.

B) The net increase of $612,000 in Research management and program services provides for $596,000 for increased emphasis in the Advanced Study areas and $38,000 for built-in items, offset by a decrease of $22,000 for payments to the NIH Management Fund.

*1974 Base - Excludes 1973 appropriation restorations. Total obligations shown in parenthesis.

Obligations by Object

	1974 Estimate	1975 Estimate	Increase or Decrease
Total number of permanent positions.....	49	49	---
Full-time equivalent of all other positions...........................	10	10	---
Average number of all employees.........	59	59	---
Personnel compensation:			
Permanent positions..................	$979,000	$1,008,000	+$29,000
Positions other than permanent........	89,000	90,000	+1,000
Other personnel compensation..........	16,000	16,000	---
Subtotal, personnel compensation....	1,084,000	1,114,000	+30,000
Personnel benefits.....................	130,000	136,000	+6,000
Travel & transportation of persons......	140,000	140,000	---
Transportation of things................	6,000	6,000	---
Rent, communications & utilities........	86,000	94,000	+8,000
Printing and reproduction..............	50,000	100,000	+50,000
Other services:			
Payment to NIH Management Fund........	243,000	221,000	-22,000
Other................................	818,000	1,148,000	+330,000
Supplies and materials..................	88,000	95,000	+7,000
Equipment...............................	28,000	35,000	+7,000
Grants, subsidies, and contributions....	2,856,000	1,695,000	-1,161,000
Total obligations by object...........	5,529,000	4,784,000	-745,000
Total obligations excluding 1973 appropriation..................	4,762,000		

Authorizing Legislation

	1975	
Legislation	Authorization	Appropriation Requested
Public Health Service Act		
Title III - General Powers and Duties of Public Health Service	Indefinite	
Part A - Research and Investigation in General (Section 301)	Indefinite	$4,784,000
International Cooperation (Section 308)	Indefinite	

John E. Fogarty International Center for Advanced Study in the Health Sciences

Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
1968	$500,000	$500,000	$725,000	$500,000
1969	600,000	600,000	600,000	600,000
1970	3,460,000	2,954,000	2,954,000	2,954,000
1971	2,664,000	3,582,000	3,582,000	3,582,000
1972	3,369,000	3,813,000	4,338,000	4,338,000
1973*	3,926,000	4,666,000	6,000,000	4,666,000*
1974	3,581,000	4,762,000	4,762,000	4,762,000
1975	4,784,000			

*Note: This appropriation authority was the continuing resolution. The appropriation amount was the House allowance, which was the lower of the House or Senate amounts in the first vetoed bill.

Justification

John E. Fogarty International Center for Advanced Study in the Health Sciences

	1974 Base*		1975 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits...........	49	$1,214,000	49	$1,250,000	---	+$36,000
Other expenses..........	---	3,548,000	---	3,534,000	---	-14,000
Total...............	49	4,762,000	49	4,784,000	---	+22,000

General Statement

The John E. Fogarty International Center for Advanced Study in the Health Sciences is designed to facilitate and expand the continuing effort of the National Institutes of Health and the United States Government to broaden the knowledge base of the biomedical sciences. The Center serves as a focal point for the international activities of the National Institutes of Health and is responsible for the administration of a number of international programs such as International Fellowships, Fogarty Scholars-in-Residence, Advanced Studies, International Visitors Center, Special Foreign Currency, and the programming of health professionals of other nations.

In administering these activities, the Fogarty International Center places its efforts on 1) facilitating the useful exchange of distinguished scientists and scholars as well as promising young scientists; 2) providing an environment, including facilities, which will contribute to the exchange, expansion and evolution of ideas; and 3) promoting international cooperation for the dissemination and sharing of biomedical knowledge both on a bilateral and multilateral basis to supplement and assist that exchange of knowledge by individual scientists and institutions.

The Fogarty International Center is requesting $4,784,000 in 1975.

*Excludes 1973 appropriation restorations.

DHEW - National Institutes of Health

CROSSWALK - 1974 COLUMN 1975 PRESIDENT'S BUDGET

INSTITUTE: John E. Fogarty International Center for Advanced Study in the Health Sciences
(in thousands of dollars)

Mechanism Program	Research Grants Specials Other	Training Programs Fellowships	Other Direct Operations	Total
1974 Base Obligations				
1. Gorgas Memorial Institute	$500			$500
2. Scholars		$1,785		1,785
3. Research Management and Program Services			$2,477	2,477
Subtotal........	500	1,785	2,477	4,762
Unobligated Balance Restored				
1. Scholars		571		571
2. Research Management and Program Services			196	196
Subtotal........		571	196	767
Total Obligations...	500	2,356	2,673	5,529

DHEW - National Institutes of Health

CROSSWALK - 1975 COLUMN 1975 PRESIDENT'S BUDGET

INSTITUTE: John E. Fogarty International Center for Advanced Study in the Health Sciences
(in thousands of dollars)

Mechanism Program	Research Grants Specials Other	Training Programs Fellowships	Other Direct Operations	Total
1. Gorgas Memorial Institute	$500			$500
2. Scholars		$1,195		1,195
3. Research Management and Program Services			$3,089	3,089
Total Obligations..........	500	1,195	3,089	4,784

John E. Fogarty International Center
for Advanced Study in the Health Sciences

Budget Mechanism

	1974*		1975	
	Number	Amount	Number	Amount
Grants				
Special				
Gorgas Memorial Institute..........	1	$500,000	1	$500,000
Total Grants........................	1	500,000	1	500,000
Fellowships				
Non-competing........................	43	427,000	---	---
Competing............................	---	---	---	---
New..................................	57	1,358,000	73	1,195,000
Supplemental.........................	---	---	---	---
Subtotal.............................	100	1,785,000	73	1,195,000
International Center.................	---	2,477,000	---	3,089,000
TOTAL................................	---	4,762,000	---	4,784,000

*Excludes 1973 appropriation restorations.

Gorgas Memorial Institute

Authorizing Legislation: Public Health Service Act Title III Part A

	1974 Base		1975 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel Compensation and benefits	---	---	---	---	---	---
Other expenses	---	$500,000	---	$500,000	---	---
Total	---	500,000	---	500,000	---	---

Introduction

The Gorgas Memorial Laboratory was organized to conduct, encourage and assist investigations in the nature and causes of tropical diseases and the methods of its prevention and treatment, and to make the knowledge relating to these subjects available for the protection of the health of the public. Situated in a tropical environment 2-1/2 hours flying time from the United States, this Laboratory offers exceptional opportunities for research and clinical training in the diseases and problems of the hot, wet tropical environments. Some diseases which are being researched include Chagas' disease, leishmaniasis, malaria, viral infections, intestinal parasites, and infantile diarrhea, all of which constitute a continuing threat to the tropical areas of the world.

Program plans 1974 and 1975

The Fogarty International Center provides the U. S. contribution to the Gorgas Memorial Laboratory which is used for maintenance and operation of the Laboratory. Additional scientific and technical support is provided from other sources. The funds provide for research in the following disciplines: virology, parasitology, malariology, serology, bacteriology, pathology, hematology, and medical entomology. The anticipated advances from this laboratory will assist in diagnosis, treatment, and management of tropical diseases which are rampant in hot climates.

Scholars

Authorizing Legislation (Public Health Service Act Title III Part A)

	1974 Base*		1975 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits..........	---	---	---	---	---	---
Other expenses.........	---	$1,785,000	---	$1,195,000	---	$590,000
Total.............	---	1,785,000	---	1,195,000	---	-590,000

Introduction

The Fogarty Scholarships Program selects outstanding scientists and other scholars who focus their attention on broad aspects of important issues raised by the findings of modern biomedical research. While in residence at the Center the scholars are encouraged by group interaction to attack broad problems, the solutions to which require an interdisciplinary approach or whose solution lies beyond the knowledge of a single individual. The program draws the scholars from the international biomedical community, and from among those people who possess special qualifications in science administration, those whose scholarly attainments suggest that they can contribute to the interactions of the group.

The unique environment at the NIH offers an unusual opportunity for scholars to interact with large numbers of intramural staff scientists in discussion--focusing attention on important health problems, holding small conferences, workshops and, on a group basis, assessing the state-of-the-art in many disease areas.

The International Research Fellowships Program offers a unique opportunity for the sharing of scientific information on an international basis by permitting foreign investigators to work for a period of a year or two in collaboration with, and in the laboratories of, American colleagues in the United States. This program provides U. S. scientists access to the ideas of vigorous young investigators with stimulating and different viewpoints. In addition, since Fellows return to do independent research in their home countries, a basis is provided for the future collaboration between investigators here and those in different environmental settings.

Program Plans in 1974 and 1975

This Program provides support to the Fogarty Scholars-in-Residence and the International Research Fellowship Programs. The Fogarty Scholars-in-Residence Program will provide opportunities to other Health Agencies of the Department to participate in this endeavor. The International Research Fellowship program will provide during Fiscal 1974 two-year fellowships which will permit a decrease in the 1975 request for this program of $590,000.

*Excludes 1973 appropriation restorations.

Research Management and Program Services

Authorizing Legislation (Public Health Service Act Title III Part A)

	1974 Base*		1975 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits............	49	$1,214,000	49	$1,250,000	---	$36,000
Other expenses............	---	1,263,000	---	1,839,000	---	+576,000
Total	49	2,477,000	49	3,089,000	---	+612,000

This activity supports the Fogarty International Center programs of advanced study, as well as the scientific, administrative and clerical staffs responsible for the overall coordination and administration of those programs.

Program Plans for 1974 and 1975

The Conference and Seminar Program provides a forum for the review and discussion of major biomedical issues confronting the nation. During the past few years, over 32 conferences have been held and the proceedings are being published and distributed. One series of conferences, on Preventive Medicine, is providing a unique opportunity for an in-depth survey of the state-of-the-art.

Other elements of the advanced study program include geographic health studies which seek to improve the nation's health by insuring that useful and pertinent knowledge developed in foreign countries is made available for consideration by U. S. medical and professional personnel. At the present time emphasis is being placed on studies on the USSR and the People's Republic of China.

The Fogarty International Center has the coordinating and policy formulation function and operating responsibility for the NIH Special Foreign Currency Program which is supported with an allotment of funds from the appropriation "Scientific Activities Overseas" managed by the Office of International Health, Office of the Secretary, DHEW.

The International Visitors Center provides an opportunity to visitors for discussion of international biomedical problems with professional staff and for the arrangement of appropriate contacts between such visitors and the Fogarty International Center and NIH staff members.

The International Education Program is responsible for arranging of professional programs for, providing supervision and consultation to, and maintaining on-going evaluation of the training experiences of World Health Organization supported medical and allied health professionals studying in the United States.

The 1975 budget provides for a net increase of $612,000. The increases consist of $38,000 in built-in items: $16,000 for within-grade pay increases; $4,000 for an extra day of pay; $2,000 for rate increases of the Bureau of Employment Compensation; $2,000 for service and supply rate increases; $14,000 for annualization of pay increases; and a program increase of $596,000 for new studies through contracts and conferences in the advanced and geographic health study areas. There is also a built-in decrease of $22,000 in payment to the NIH management fund.

*Excludes 1973 appropriation restorations.

NATIONAL INSTITUTES OF HEALTH

John E. Fogarty International Center
for Advanced Study in the Health Sciences

Program Purpose and Accomplishments

Activity: Research grants (Public Health Service Act Title III Part A)

1974			1975 Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
---	$500,000	Indefinite	---	$500,000

Purpose: This grant provides the legislatively authorized U.S. contribution for the operation and maintenance of The Gorgas Memorial Laboratory now comprising the merged facilities of the former Middle America Research Unit and The Gorgas Memorial Laboratory. The purpose of this institution is to conduct research on tropical diseases of public health importance to the United States and Latin America, to provide guidance for the application of research findings to preventive and therapeutic ends and to provide education opportunities for students of tropical medicine.

Accomplishments in 1974: During fiscal year 1974 The Gorgas Memorial Laboratory continued research on malaria, trypanosomiasis, leishmaniasis, bacterial diarrheas and arboviruses of public health importance. Major accomplishments include the adaptation of human malaria parasites to indigenous simian species and the initiation of experimental chemotherapy in these hosts; the recognition of the major insect vector of trypanosomiasis in virgin forest; new mammalian hosts for the three species of leishmania in Panama; further study of ecologic derangement in the Bayano River impoundment area; attenuation of a potential vaccine strain of Bolivian Hemorrhagic Fever virus; identification of in-vitro markers of VEE virus isolates of differing virulence; six new viruses from phlebotomine flies; serologic evidence of dengue virus activity in man; and serologic evidence of recurrence of sylvan yellow fever. Training of postdoctoral candidates continued under the aegis of university exchange and military medicine programs.

Objectives in 1975: The Gorgas Memorial Laboratory proposes to exploit fully current findings in experimental malaria in simian models, studies of immunity in human infection with trypanosomes and leishmania, further evaluation of attenuated vaccine candidates of BHF virus and studies of ecology of VEE, sand fly viruses and yellow fever. Current activities include major efforts to contain recurrent human yellow fever and the attendant risk of urban outbreaks.

NATIONAL INSTITUTES OF HEALTH

John E. Fogarty International Center
for Advanced Study in the Health Sciences

Program Purpose and Accomplishments

Activity: Scholars (Public Health Service Act Title III Part A)

1974			1975 Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
---	$1,785,000	Indefinite	---	$1,195,000

Purpose: The Fogarty Scholars-in-Residence Program provides outstanding scientists and other scholars the opportunity to focus their attention on broad aspects of important issues raised by the findings of modern biomedical research. While in residence at the Center the scholars are encouraged by group interaction to attack broad problems, the solutions to which require an interdisciplinary approach or whose solution lies beyond the knowledge of a single individual. Fogarty Scholars-in-Residence through the unique environment at NIH have an unusual opportunity to interact with a large number of intramural staff scientists in discussions of various problems within their specific discipline, such as biochemistry, physiology, etc., particularly as they relate to cancer and cardiovascular research.

The International Postdoctoral Fellowships Program offers a unique opportunity for the sharing of scientific information on an international basis by permitting foreign investigators to work for a period of a year or two in collaboration with, and in the laboratories of, American colleagues in the United States. This program provides U. S. scientists access to the ideas of vigorous young investigators with stimulating and different viewpoints. In addition, since Fellows return to do independent research in their home countries, a basis is provided for the future collaboration between investigators here and those in different environmental settings.

Accomplishments in 1974: In 1974, 100 awards were made to individuals in order to engage in collaborative research with American scientists on health problems of mutual interest and to advance the basic knowledge in the biomedical sciences, in such areas as molecular biology, cell biology, genetics, neurophysiology, endocrinology and others.

Objectives in 1975: In 1975, 73 awards will be made to applicants whose research proposals will have a direct effect upon research in the disciplines such as cell biology, biochemistry, physiology and other biomedical fields as they may apply to cancer, cardiovascular diseases, neurological diseases, medical genetics, metabolic diseases and others.

NATIONAL INSTITUTES OF HEALTH

John E. Fogarty International Center
for Advanced Study in the Health Sciences

Program Purpose and Accomplishments

Activity: Research management and program services (Public Health Service Act Title III Part A)

1974			1975 Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
49	$2,477,000	Indefinite	49	$3,089,000

Purpose: The John E. Fogarty International Center for Advanced Study in the Health Sciences is designed to facilitate and expand the continuing effort of the National Institutes of Health and the United States Government to broaden the knowledge base of the biomedical sciences. The Center serves as the focal point for the international activities of the National Institutes of Health. The Center also is responsible for the administration of a number of international programs such as International Fellowships, Scholars-in-Residence, Advanced Study, International Visitors Center, Special Foreign Currency, and programming of health professionals of other nations.

Accomplishments in 1974: Results of the Fogarty Center sponsored studies on various aspects of preventive medicine will be published early in 1975. This timely subject has received increased attention during the past several years and these publications will contribute to the knowledge base for further examination. Other studies, particularly studies of medicine and public health in the Soviet Union and the People's Republic of China have resulted in publications which are being added to the curriculum of Schools of Medicine and Public Health.

Objectives in 1975: Increased emphasis in the advanced study area, either through individual studies or conferences, workshops and seminars, will permit further analyses and comparative studies of medicine and public health and the exchange of scientific and biomedical knowledge.

MONDAY, APRIL 1, 1974.

NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES

WITNESSES

DR. DAVID P. RALL, DIRECTOR
DR. ROBERT S. STONE, DIRECTOR, NATIONAL INSTITUTES OF HEALTH
GEORGE M. KINGMAN, EXECUTIVE OFFICER, NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES
BENJAMIN A. ORRINGER, BUDGET OFFICER, NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES
LELAND B. MAY, ACTING DIRECTOR OF FINANCIAL MANAGEMENT, NATIONAL INSTITUTES OF HEALTH
WILFORD FORBUSH, DIRECTOR, OFFICE OF BUDGET, HEALTH, EDUCATION, AND WELFARE

Object Classification (in thousands of dollars)

Identification code 09-25-0862-0-1-651		1973 actual	1974 est.	1975 est.
	Personnel compensation:			
11.1	Permanent positions	3,316	3,567	3,572
11.3	Positions other than permanent	413	587	625
11.5	Other personnel compensation	82	110	120
	Total personnel compensation	3,811	4,264	4,317
12.1	Personnel benefits: Civilian	361	436	441
21.0	Travel and transportation of persons	275	320	350
22.0	Transportation of things	25	27	30
23.0	Rent, communications, and utilities	936	980	990
24.0	Printing and reproduction	43	50	60
25.0	Other services	4,025	4,180	4,692
26.0	Supplies and materials	1,079	897	1,390
31.0	Equipment	589	500	600
41.0	Grants, subsidies, and contributions	14,993	21,468	15,814
99.0	Total obligations	26,137	33,122	28,684

Personnel Summary

	1973 actual	1974 est.	1975 est.
Total number of permanent positions	248	236	235
Full-time equivalent of other positions	76	90	95
Average paid employment	311	331	328
Average GS grade	8.5	8.6	8.6
Average GS salary	$14,260	$15,138	$15,473
Average salary of ungraded positions	$11,138	$12,018	$12,253

Program and Financing (in thousands of dollars)

	Identification code 09–25–0862–0–1–651	1973 actual	1974 est.	1975 est.
	Program by activities:			
	1. Environmental health sciences centers	3,556	4,000	5,100
	2. Environmental mutagenesis and reproductive toxicology	1,762	3,015	2,800
	3. Etiology of environmental diseases and disorders	4,743	5,646	4,100
	4. Environmental pharmacology and toxicology	5,420	7,865	4,334
	5. Environmental pathogenesis	1,626	2,942	1,810
	6. Intramural laboratory and clinical research	8,053	8,275	9,158
	7. Research management and program services	1,436	1,379	1,382
	Total program costs, funded [1]	26,596	33,122	28,684
	Change in selected resources (undelivered orders)	−459		
10	Total obligations	26,137	33,122	28,684
	Financing:			
25	Unobligated balance lapsing	4,823		
	Unobligated balance restored		−4,736	
	Budget authority	**30,960**	**28,386**	**28,684**
	Budget authority:			
40	Appropriation	30,956	28,879	28,684
	Withheld from obligation and expenditure (Public Law 93–192)		−482	
41	Transferred to other accounts		−11	
42	Transferred from other accounts	4		
43	**Appropriation (adjusted)**	**30,960**	**28,386**	**28,684**
	Relation of obligations to outlays:			
71	Obligations incurred, net	26,137	33,122	28,684
72	Obligated balance, start of year	15,466	15,193	16,945
74	Obligated balance, end of year	−15,193	−16,945	−12,020
77	Adjustments in expired accounts	−561		
90	Outlays	25,849	31,370	33,609

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[1] Includes capital outlay as follows: 1973, $743 thousand; 1974, $630 thousand; 1975, $650 thousand.

NOTES

Includes $29 thousand in 1975 for activities previously financed from (in thousands of dollars):

	1973	*1974*
National Institute of General Medical Science	24	24
Departmental Management	1	1

Excludes $30 thousand in 1975 for activities transferred to the Office of Assistant Secretary for Health: 1973, $30 thousand; 1974, $30 thousand.

Excludes $11 thousand in 1974 and 1975 for activities transferred to Departmental Management. Comparable amount for 1973 ($11 thousand) is included above.

WITNESS INTRODUCTION

Mr. FLOOD. The committee will come to order.

We are very pleased to have present today some distinguished visitors who are scientists from the Soviet Republic and we are very happy they are here.

We are especially pleased to note they are scientists and interested in the environmental sciences primarily, although we understand they are not limiting their visits to our department just to environmental sciences but to other departments related to that subject as well.

I have a number of constituents in my district whose ancestors come from various parts of Russia and I do not talk very good Russian. All I know are all the bad words.

We now have the National Institute of Environmental Health Sciences. The presentation will be made by Dr. David P. Rall, the Director. I see we have your biographical sketch which we will place in the record.

[The biographical sketch follows:]

BIOGRAPHICAL SKETCH

Name: David P. Rall, doctor of medicine, doctor of philosophy.

Position: Director, National Institute of Environmental Health Sciences.

Birthplace and date: Aurora, Ill., August 3, 1926.

Education: Bachelor of arts, North Central College, 1946; master of science, Northwestern University, 1948; doctor of philosophy, Northwestern University, 1951; doctor of medicine, Northwestern University, 1951.

Experience: Director, National Institute of Environmental Health Sciences, 1971–present. Associate Scientific Director for Experimental Therapeutics, National Cancer Institute, 1966–71. Chief, Laboratory of Chemical Pharmacology, National Cancer Institute, 1963–69. Head, Clinical Pharmacology and Experimental Therapeutics Service, General Medicine Branch, National Cancer Institute, 1958–63.

Scientist, Clinical Pharmacology and Experimental Therapeutics Service, General Medicine Branch, National Cancer Institute, 1955–58. Scientist, Laboratory of Chemical Pharmacology, National Cancer Institute, 1953–55. Research Associate in Pharmacology, Northwestern University, 1950. Assistant in Pharmacology, Northwestern University, 1949–50. Baxter fellow in pharmacology, Northwestern University, 1947–49.

Association memberships: Fellow, American Association for Advancement of Science. Society for Experimental Biology and Medicine. American Society for Pharmacology and Experimental Therapeutics. American Association for Cancer Research. American Society for Clinical Investigation. Federation of American Societies for Experimental Biology. Society of Toxicology. American Occupational Health Society. American Society for Clinical Pharmacology and Therapeutics.

Special awards, citations, or publications: Editorial Board, Archives of Environmental Health, 1973-present. Chairman, DHEW Committee to Coordinate Toxicology and Related Programs. U.S. Coordinator. Environmental Health Program, U.S.-U.S.S.R. Health Exchange Agreement, 1972-present. U.S. Coordinator, Biological and Genetic Consequences Project, U.S.-USSR Environmental Protection Agreement, 1972-present. U.S. Coordinator, U.S.-U.K. Cooperative Program in Environmental Health Sciences, 1972-present. Chairman, OST–CEQ, ad hoc Committee on Environmental Health Research, 1971–72.

Chairman, HEW Departmental Committee on Drug Research and Regulations, 1970. Editorial Board, Pharmacological Reviews, 1969-present. Chairman, National Institute of General Medical Sciences Pharmacology-Toxicology Review Committee, 1967–69. Member, Graduate Council, George Washington University, 1962-present. Editorial Board, Proceedings of the Society for Experimental Biology and Medicine, 1962–65. Lecturer in Physiology, Medical School, George Washington University, 1958–62. Meritorious Service Medal; Dr. Rall has authored and coauthored over 100 published papers relating to comparative pharmacology, cancer chemotherapy, blood-brain barrier, blood CSF barrier, pesticide toxicology, and drug research and regulation.

Mr. FLOOD. Is there anybody you would like us to meet?

Dr. RALL. I would like to introduce our executive officer, Mr. George Kingman, and our budget officer, Mr. Al Orringer.

Mr. FLOOD. I see you have a prepared statement, Doctor. How do you want to handle this?

Dr. RALL. May I read it for you?

Mr. FLOOD. It is up to you.

OPENING STATEMENT

Dr. RALL. Thank you. Mr. Chairman and members of the committee, it is a pleasure to appear before you again on behalf of the National Institute of Environmental Health Sciences to discuss our budget request for the forthcoming year.

INSTITUTE MISSION

It is the responsibility of the National Institute of Environmental Health Sciences to develop new knowledge through research to protect us from the introduction into the environment—or continued use—of those environmental agents which are health hazards. NIEHS developed knowledge is used to guide regulatory action and to serve as the foundation for preventive and therapeutic programs.

Biomedical research into the nature of diseases and preventive programs produce significant long-term benefits for all of us. While curative advances, such as new drugs and heart transplants, are dramatic, preventive measures, such as vaccines, have clearly contributed more to the maintenance and improvement of the Nation's health. While curative medicine is the last defense against disease, preventive medicine is the first. And it is only through prevention that we can insure personal health and, subsequently, reduce the enormous financial burden of health care.

Fundamental research conducted and supported by NIH's National Institute of Environmental Health Sciences is designed to serve as the basis for preventive programs for environmentally-related diseases. Awareness of the importance of this research has grown steadily in recent years as a result of the realization that man's health is intimately linked to his environment. Long-term, low-level exposures to many chemical, biological and physical environmental agents are known to adversely affect man's health. To understand the effects of such exposures, to provide the medical community the best possible information on the toxic effects of environmental agents, and to aid in the development of programs to prevent these exposures, NIEHS carries out a broad and coordinated effort in environmental health research.

The new knowledge developed through NIEHS research is also used to provide the various regulatory agencies with the scientific bases for the best possible regulatory action. While control agencies can control many environmental problems through regulatory action, the nature of our society is such that it is often not feasible to do so. This is because our whole economic and social structure is dependent upon the widespread use of modern technology. The energy shortfall is an immediate example of a situation where compromise and tradeoffs are essential to maintain a vigorous economy. Thus, most of our environmental problems can only be ameliorated, not eliminated, by regulation. Therefore, the scientific base of knowledge developed by NIEHS is essential to rational and effective regulatory action and, most importantly, to the development of effective preventive measures.

RESEARCH PROGRAMS

To carry out our efforts in environmental health research, we employ a variety of support mechanisms in order to involve the Nation's highly qualified scientists in our work. Our intramural laboratory and clinical programs and our grant-supported Environmental Health Sciences Centers and program projects and individual project grants all contribute to our various research programs. These programs include: environmental mutagenesis and reproductive toxicology, etiology of environmental diseases and disorders, environmental pharmacology and toxicology, and environmental pathogenesis.

To illustrate the types of problems with which the NIEHS is concerned, I would like to discuss these programs, as well as examples of NIEHS supported fundamental research which we believe have potential importance for the health of every American.

ENVIRONMENTAL MUTAGENESIS AND REPRODUCTIVE TOXICOLOGY

Changes in hereditary factors and in the capacity to produce viable, productive and intelligent progeny are potential hazards associated with environmental pollution. Our program in this area is concerned with developing understanding of the nature of mutagenic and teratogenic agents—or those capable of producing inheritable changes and birth defects—and other compounds that might affect developmental and physiological characteristics of man. A major effort is being made to develop and refine methodology for evaluation of man's exposure to such agents.

Evidence accumulated through several decades leaves little question of the genetic hazard of many of the products and byproducts of contemporary technology and of a substantial number of chemical agents of natural origin. Moreover, there is growing conviction among scientists that genetic damage probably contributes to inherent susceptibility to disease and may indeed be causal in some types of cancer.

One mutagenic agent which illustrates our concerns and work in the area of environmental mutagenesis is the nitrofuran derivative AF–2 which, fortunately, has not been approved by the FDA for use in this country. Problems resulting from the use of this compound point out dramatically that we need to develop more precise and rapid methods to screen chemicals prior to their release. In addition, we need to develop better methods to monitor the population and evaluate the extent of genetic damage produced in individuals and the population as a result of accidental exposure to mutagens.

AF–2 has been used as a food additive in Japan since 1965. Its mutagenic properties were discovered by accident recently, resulting in widespread concern because AF–2 is believed to be one of the most potent compounds ever discovered. The major concerns are twofold. First, we do not have at our disposal any completely adequate methods to determine whether significant levels of genetic damage have been produced in either somatic or germ cells of exposed individuals. Second, even though we could look for an increased frequency of chromosome damage in cultured blood samples from exposed persons, we do not have suitable control groups with which to compare our findings. This is because virtually the entire population of Japan has been exposed to AF–2 via its addition to several foods that are Japanese staples. Thus, we could not answer one of the major questions: are the chromosome aberration levels found due to AF–2 or do they represent the spontaneous level found in the Japanese population?

NIEHS is concerned that there are no completely adequate methods to determine directly the level of genetic damage produced in popultion inadvertently exposed to mutagenic agents. Consequently, we have initiated projects and are making progress in developing a simple assay to monitor the human population for gene mutations, as well as in developing and refining other methodology. We are also attempting to stimulate other research in this area and to search out areas of expertise abroad. For example, we are collaborating with three strong laboratories in Germany which are working on new and better methodology for detecting genetic damage. Cooperation is also underway with scientists in England and Japan; and we are just beginning a similar cooperative program with scientists in the Soviet Union.

In the area of reproductive toxicology, our scientists have developed a technique for recovering embryos (the developing stage of an organism) from mice, rats and rabbits, culturing them in test tubes, exposing them to chemicals, and then reimplanting them in foster mothers where they remain viable to term. Chemicals whose effects are well known—such as thalidomide—are being used to validate this procedure.

We have found that this technique makes possible the direct exposure of mammalian embryos to test agents, thereby bypassing maternal influences and permitting us to distinguish between direct and indirect insults on embryo development. It also enables us to determine the effects of various chemical and physical agents, acting alone or in combination, on subsequent development.

This and related experimental approaches are being used to increase our understanding of embryonic requirements for development and to determine whether some of the unexplained birth defects might result from enhanced environmental stress on the mother. We plan to continue our investigations of classic teratogens and environmental agents to determine the potential of this approach in resolving some of the problems involved in extrapolating experimental results to humans.

ETIOLOGY OF ENVIRONMENTAL DISEASES AND DISORDERS

The principal aim of this program is to clarify the causative role environmental agents play in human disorders and to assess the potential hazard of numerous new environmental compounds. Such knowledge is the first defense in our efforts to protect man from adverse health effects.

One environmental hazard which has been studied under this program involves a family of organic chemicals commonly called halo ethers. These compounds are used in large quantities in the chemical industry for polymerization and stabilization of polymers. Last year I discussed one of these compounds—bis chloromethyl ether. At that time a team of scientists supported by an NIEHS Center grant at the New York University Institute of Environmental Medicine had discovered that bis chloromethyl ether presented a significant carcinogenic hazard to human health.

The ultimate benefit of this NIEHS-supported basic research on bis chloromethyl ether lies not only in the fact that a dangerous compound and industrial situation were identified, but also in the fact that we were alerted to the possibility that other halo ethers could be hazards in the general environment. Because other Federal agencies were informed of this possibility, the EPA was able to identify a potential human health hazard when several halo ethers recently were found in river water in various places. Effective steps now can be taken to limit exposure to save lives.

ENVIRONMENTAL PHARMACOLOGY AND TOXICOLOGY

Overt manifestations of environmental diseases and mutational events are more dramatic and capture public interest, but the tools for preventing and treating disease can be provided only by fundamental research. To provide the necessary knowledge, research conducted under this program deals with the questions of how and why toxic agents produce recognizable disease endpoints. An example of this research is the study by Institute scientists of the pulmonary effects of compounds common to household aerosols.

The widespread use of the aerosol "spray can" dispenser has resulted in very complex and wide variety of materials being available in respirable form. While the acute toxicity of many of the "active ingredients" in such dispensers has been investigated, little is known about the chronic toxicity of these compounds, or the toxicity of combinations of these compounds and "inert ingredients" of the pressurized cans.

In our studies, exposures of rats, rabbits, and hamsters to aerosols of aluminum chloride-hydroxide, a constituent of virtually all deodorant sprays, have produced increases in lung weights and damage to air passages in the lungs. Some of the fluorocarbons (Freons), which are the propellant gases and solvents in aerosol sprays, have been shown to depress certain heart functions, such as the contractility of the normal heart muscle. In addition, toxicity studies in progress indicate that certain chemicals in widespread use may be highly toxic to animals with preexisting heart disease or respiratory imbalance.

Another example of research in this area concerns the polychlorinated biphenyls (PCB's), a class of industrial chemicals which contaminate this country's waterways. The ability of marine species to detoxify and/or excrete these compounds, as well as the chemically related pesticides, may well play an important role in whether or not such animals can continue to be used as a safe food source for humans.

Our studies have shown that the PCB's are not concentrated in most of the edible tissues in fish and seafood. For example, the muscle masses of the lobster are very low in PCB or DDT content, while organs of excretion concentrate and store these pollutants. Thus, by discarding organs of excretion of the lobster, we could retain most of the edible portions for human consumption.

ENVIRONMENTAL PATHOGENESIS

This program endeavors to describe in detail and in time sequence the molecular and cellular events that culminate in recognizable diseases and disorders. The knowledge developed offers the best hope, aside from prevention of exposure, of detecting and countering pathologic processes before damage becomes irreversible.

One of our areas of concern is pulmonary disorders. Scientists at the University of Cincinnati have conducted extensive studies on the pulmonary effects of coal dust and the role of specific components of the dust in the etiology and pathogenesis of pneumoconiosis (a chronic fibrous reaction in the lungs due to the inhalation of dust.) They have shown that there are quantitative differences in chemicals which can be extracted from bituminous coal from mines in Pennsylvania and Utah.

Mr. Flood. What about the hard coal, anthracite?

Dr. Rall. They are beginning to look at anthracite.

Mr. Flood. Isn't that nice. Every time they mention coal in this town all they can think of is bituminous. They can't spell anthracite. Not only can't you spell it but you omitted it entirely.

Dr. Rall. We are aware of the anthracite problem. We are planning studies on that.

Mr. Flood. In the next 10 minutes?

Dr. Rall. No, but soon.

Mr. Flood. That's a hint. Can you take a cue?

Dr. Rall. Yes, indeed.

Mr. Flood. Proceed.

Dr. Rall. The most striking chemical differences are in nickel and iron contents, with the Pennsylvania coal being substantially higher in both. Correlates between the incidence of pneumoconiosis in miners in Pennsylvania and Utah show that the former is significantly higher, which is in accord with the high nickel and iron content of the coal. Moreover, experiments with cultured cells show that extracts from Pennsylvania coal are substantially more toxic than those of Utah coal, which parallels the nickel content in both cases.

Although these studies must be viewed as only suggestive, other data in the literature on nickel indicate that this metal is indeed highly toxic by all routes of administration in intact animals and to all types of cells with which it comes into direct contact. It appears, therefore, to warrant more intensive study, particularly as a pulmonary hazard.

Mr. Flood. I want to say again at this point, for the purpose of emphasis, anthracite we call hard coal. Now that term is self-definitive. It would seem to me like night follows day that you would be especially concerned about the effect of the particles of hard coal vis-a-vis that of soft coal. It is a question of degree. There is no doubt that the particles of hard coal without doubt just physically are more deleterious. I would expect you would give rather immediate attention to all facets of that problem.

Dr. Rall. We are. Since we will need both all of the hard and soft coal we can get in the future we will study this problem very carefully indeed.

LIAISON AND COMMUNICATION OF FINDINGS

In the environmental health field, liaison and communication of findings are vital. One way we have carried out our responsibilities in this area is through sponsorship of a series of meetings on current problems in environmental health. We believe these meetings to be invaluable as they provide a neutral ground for regulatory agencies, regulated industry, academic scientists, and science writers to meet and hear a comprehensive review of the latest information on a current and specific problem. They have been extremely successful in providing a balanced perspective on current environmental problems and in increasing our environmental health sciences centers, our grants and contracts programs in environmental mutagenesis and reproductive toxicology, and our intramural research program in the areas of enenvironmental mutagenesis and reproductive toxicology and etiology of environmental diseases and disorders.

I shall be pleased to try to answer any questions and supply any additional material desired for the record.

BUDGET REQUEST

Mr. Flood. As you say, Doctor, you are requesting a budget of $28,684,000 for fiscal year 1975. That is an increase of $346,000 over 1974. Is that correct?

Dr. Rall. That is correct.

Mr. Flood. In the current fiscal year, 1974, you have received $4.7 million of restored 1973 funds. How did you spend that money?

Dr. Rall. That money went for research grants, program projects, and training grants. It was divided among the various program areas of etiology, pharmacology, toxicology, and pathology as the major areas in grants.

Mr. Flood. You better have the record show something on that.

Dr. Rall. We will.

[The information follows:]

NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES—DISTRIBUTION OF 1973 IMPOUNDED FUNDS

[Amounts in thousands]

Budget mechanism	Number of awards	Amount
Research grants	51	$3,147
Environmental mutagenesis and reproductive toxicology	(13)	(797)
Etiology of environmental diseases and disorders	(14)	(866)
Environmental pharmacology and toxicology	(17)	(1,056)
Environmental pathogenesis	(7)	(428)
Fellowships	2	15
Environmental pharmacology and toxicology	(2)	(15)
Training grants	2	1,202
Environmental mutagenesis and reproductive toxicology		(36)
Etiology of environmental diseases and disorders	(2)	(288)
Environmental pharmacology and toxicology		(757)
Environmental pathogenesis		(121)
Research and development contracts		

MULTIYEAR GRANTS

Mr. Flood. Did you, or are you, going to make any of these multiyear grant awards, 2 years or more, in 1974?

Dr. Rall. We plan to do a very modest amount of multiyear grant awarding in 1974, but by multiyear, this to us can mean as little as 13 months. We will probably have about 18 such awards in 1974.

Mr. Flood. For the record, look at page 143 of your justifications. What we want is a revision of that table on page 143. Specifically, we want to see included in the 1974 column the restored 1973 funds and the impact of those funds, of course, on fiscal 1975. We have asked all of the other Institutes exactly the same questions.

Dr. Rall. Yes.

[The information follows:]

National Institute of Environmental Health Sciences

Obligations by Budget Mechanism Showing "True" Program Levels in 1974 - 1975

(Amounts in thousands)

Budget Mechanism	1972		1973		1974		1975	
	No.	Amount	No.	Amount	No.	Amount	No.	Amount
Grants								
Regular:								
Non-competing	76	$5,667	100	$6,286	91	$6,270	144	$8,406
Competing	19	1,319	13	1,327	22	1,423	9	608
New	33	1,661	25	1,195	76	3,771	22	992
Supplemental	(7)	319	(5)	66	(4)	65	(5)	75
Subtotal	128	8,966	138	8,874	189	11,529	175	10,081
Special:								
Environmental health sciences centers	6	3,389	6	3,743	6	4,000	7	5,100
Research career programs	8	180	9	182	9	199	9	195
Scientific evaluation	---	24	---	24	---	24	---	28
Subtotal	14	3,593	15	3,949	15	4,223	16	5,323
Total Grants	142	12,559	153	12,823	204	15,752	191	15,404
Fellowships:								
Non-competing	9	70	---	5	3	31	39	593
Competing	---	---	---	---	---	---	---	---
New	3	24	3	22	39	575	33	482
Supplemental	---	---	---	---	---	---	---	---
Subtotal	12	94	3	27	42	606	72	1,075
Training Grants:								
Non-competing	22	2,121	23	1,670	21	2,195	18	700
Competing	8	900	4	207	1	48	---	---
New	---	---	0	0	1	60	---	---
Supplemental	(7)	66	(6)	100	(1)	1,094	---	---
Scientific Evaluation	(1)	20	(1)	18	---	---	---	---
Subtotal	30	3,107	27	1,995	23	3,397	18	700
Laboratory & clinical research	---	6,604	---	7,813	---	8,203	---	9,158
Research & development contracts	---	2,300	---	1,851	---	2,000	---	2,330
Research management & program services	---	1,222	---	1,345	---	1,379	---	1,382
TOTAL	184	25,886	183	25,854	269	31,337	281	30,049

NATIONAL INSTITUTES OF HEALTH

National Institute of Environmental Health Sciences

Obligations by Budget Activity
Showing "True" Program Levels
in 1974 - 1975
(Amounts in thousands)

Budget Program	1973		1974		1975	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
E.H.S. Centers..................................	---	$3,743	---	$4,000	---	$5,100
Environmental mutagenesis & reproductive toxicology..................................	---	1,670	---	2,685	---	3,098
Etiology of environmental diseases & disorders...	---	4,472	---	5,135	---	4,504
Environmental pharmacology & toxicology..........	---	5,134	---	7,247	---	4,796
Environmental pathogenesis.......................	---	1,677	---	2,688	---	2,011
Intramural laboratory & clinical research........	195	7,813	197	8,203	197	9,158
Research management & program services...........	38	1,345	38	1,379	38	1,382
TOTAL NIEHS...........	233	25,854	235	31,337	235	30,049

National Institute of Environmental Health Sciences

Multi-Year Funding from 1974 Appropriation

(Amounts in thousands)

Budget Mechanism	No. of Awards	Amount	Amount Affecting 1975 Funding	Remarks
Research Grants....................	18	$1,794	$897	
	(4)	(438)	(219)	Environmental mutagenesis & reproductive toxicology
	(5)	(496)	(248)	Etiology of environmental diseases & disorders
	(6)	(611)	(306)	Environmental pharmacology & toxicology
	(3)	(249)	(124)	Environmental pathogenesis
Fellowships........................	--	--	--	
Training Grants....................	--	--	--	
Research and Development Contracts..	--	--	--	

COORDINATION WITH OTHER AGENCIES

Mr. Flood. Back and forth we have discussed this subject of the relationship of your shop with other agencies. We have talked about that quite a good deal in the past every year. The reason we are raising it again this year is because it is still unclear as to how you relate to these other outfits and to avoid one of our pet hates—avoid duplication of effort with the following agencies:

The Cancer Institute. Here we talk about lung cancer and so on. What about that? Tell us something about that. How do you relate with these people?

Dr. Rall. We relate at a variety of different levels. I relate pretty well with the Cancer Institute. I was on the Cancer Institute staff for 17 years. So I know the personnel very well indeed. But we have formal mechanisms whereby the research directors talk to each other so that we know what research is going on in each other's shops.

It seems to us that this sort of discussion of research across institute lines is the most effective way of creating very good collaboration and avoiding any possible duplication.

In addition, Dr. Stetten has introduced a new system whereby each scientific director will spend a half a day discussing his research with Dr. Stetten and also representatives of the other NIH Institutes.

Mr. Flood. We are getting a lot of flak on this lately, as you know, the National Institute of Occupational Safety and Health. That is red hot now. What about that?

Tell us briefly now how you relate to these other people, then when you get the record back as you see fit in your judgment you may wish to develop what you said in certain areas.

TOXICOLOGY COORDINATING COMMITTEE

Dr. Rall. Yes, indeed.

Dr. Edwards about 9 months ago, I think, felt much, as you do, the need to coordinate the various toxicological programs in HEW, and he established a HEW committee to coordinate toxicology and related matters.

This committee, of which I am the chairman, has two representatives from NIOSH, three or four representatives from NIH, not only NCI but also the National Institute of General Medical Sciences, the Food and Drug Administration and the other relevant groups within HEW.

We have been meeting at monthly intervals, presenting our own research programs, discussing current problems as we see them, trying to develop approaches to solving these problems by working together in a cooperative and nonduplicative sort of way.

Mr. Flood. And you are aware of the heat and the pressure that is on this particular thing just now?

Dr. Rall. Absolutely, and we work very closely with Dr. Key and his colleagues. We attend each other's major meetings and are on the telephone all of the time with them.

Mr. Flood. What about the Institute of General Medical Sciences? They have cellular and molecular research.

Dr. Rall. Two representatives of that Institute are on the toxicology coordinating committee, have met with us constantly and have been down to visit with us in North Carolina. We have heard presentation of their research programs. The coordination is good at the scientist-to-scientist level and we are trying hard to be sure that at the administrative levels there is coordination as good as that at the scientist-to-scientist level.

REPRODUCTIVE TOXICOLOGY

Mr. FLOOD. What about the National Institute of Child Health and Human Development? There you have the reproductive toxicology. What about the relationship there?

Dr. RALL. They are not represented specifically on this committee. We, however, are in the process of setting up a subcommittee of this committee which will deal with what we call teratology, birth defects and so forth. This subcommittee will bring in those people from child health who are interested. There is a group in the Dental Institute that is concerned about birth defects that affect the mouth and face such as cleft palate. This new subcommittee is patterned after a subcommittee of the DHEW Committee to Coordinate Toxicology and Related Programs which has been in existence for about 9 months on mutagenesis. This committee includes all of the relevant scientists within HEW as well as observers, not members but observers from the other agencies in the Government.

Mr. FLOOD. What about the always present and always front and center National Heart and Lung Institute where you have the pulmonary and cardiovascular systems? How do you work with them?

Dr. RALL. The same way. We don't have a specific committee for them but we work very closely with them.

Mr. FLOOD. The reason we touch on these things is, as you know, you probably have the message, we believe very strongly you have to achieve coordination between these programs in order to avoid that duplication of effort. It is the old story—only so many dollars and how you are going to cut up that pie. We want to be sure the taxpayer is getting the maximum amount of return possible in this business of research. You are under the guns as you know.

CHARTER OF COORDINATED TOXICOLOGY COMMITTEE

Dr. RALL. I would be delighted to submit for the record the charter of the toxicology coordinating committee which I think addresses itself to this question.

[The information follows:]

CHARTER

DHEW COMMITTEE TO COORDINATE TOXICOLOGY AND RELATED PROGRAMS

PURPOSE

The DHEW Committee to Coordinate Toxicology and Related Programs, hereinafter referred to as the Coordinating Committee, is established by the Assistant Secretary for Health, DHEW, as a multi-Agency group to provide a medium to assure exchange of information on toxicology and related programs, to coordinate these programs, to enhance sharing of resources, and to provide advice to the Department.

SCOPE

The advice that is to be provided to the Department by the Coordinating Committee shall aid in determining the allocation of resources among goals and activities in toxicology and related programs, and shall serve to guide the decisions being made by the regulatory Agencies and the Assistant Secretary for Health in respect to new and unforeseen problems.

The Committee and its individual members shall serve also as points of contact with the scientific and industrial communities and with state and local governments, both to receive and to provide information and advice on toxicology and related matters of mutual interest and concern.

The Committee shall consist of a high level representative and an alternate from each Agency within the Department of Health, Education, and Welfare supporting or conducting toxicology or related programs.

In each case, the representative of a member Agency must be knowledgeable of his/her Agency's technical activities and must be able to speak authoritatively for the Agency or promptly gain the response of the Agency's ultimate authority in order to assist in the assignment of priorities and the solution of urgent and unforeseen problems.

STRUCTURE

The members of the Committee, and their alternates, shall be proposed by the following, and appointed by the Assistant Secretary for Health; Director, Office of Program Operations in the Office of the Assistant Secretary for Health; Director, National Institutes of Health; Director, National Cancer Institute; Director, National Institute of Environmental Health Sciences; Director, National Institute of Mental Health; Director, National Library of Medicine; Director, Center for Disease Control; Director, National Institute of Occupational Safety and Health; Commissioner, Food and Drug Administration; and Director, National Center for

Toxicological Research. The chairman of the Committee shall be selected by the Assistant Secretary for Health from among the members of the Committee. The executive secretary shall be provided by the Office of Program Operations in the Office of the Assistant Secretary for Health.

Staff support shall be provided jointly by the Office of Program Operations (OASH), the office of the chairman of the Committee and by each of the member Agencies represented on the Committee.

A steering subcommittee shall be established to guide the work of the Committee in a manner suited to the needs of the Department. The Steering Subcommittee shall achieve its purpose by developing agendas which are most germane to the needs of the Department and by ensuring a brisk pace in the resolution of problems. The chairman of the Committee shall serve also as chairman of the Steering Subcommittee. The members of the Steering Subcommittee shall be the principal member of the Committee from one of the research organizations in DHEW and the principal members of the Committee from two of the regulatory Agencies in the Department.

MEETINGS

It is expected that the Coordinating Committee shall meet regularly about six times per year, although there may be need to meet at other times to deal with urgent and unforeseeable problems on which the Assistant Secretary may be seeking advice.

MANAGEMENT CONTROL FUNCTIONS

Management Control Functions for the Committee shall be performed in the Office of Special Projects, in the Office of Program Operations, Office of the Assistant Secretary for Health, DHEW.

REPORTS

The Coordinating Committee shall report to the Assistant Secretary for Health, DHEW, through the Director, Office of Program Operations, and the Deputy Assistant Secretary for Health. Annual reports shall be submitted to the Assistant Secretary for Health June 30; interim reports shall be submitted as necessary.

DURATION

The duration of the Committee is expected to be two years from date of approval.

APPROVED:

7/17/73

s/Charles C. Edwards
Assistant Secretary for Health

IDENTIFICATION OF HAZARDOUS SUBSTANCES IN THE WORK ENVIRONMENT

Mr. FLOOD. How much of your budget is spent on research to identify the potentially hazardous substances in the industrial and work environment? I don't know if you have that with you right now. If not, you certainly must have it in the record. The direct question is how much of your budget is spent for that work? If you don't have the figure, put it in the record.

[The information follows:]

The primary mission of the National Institute of Environmental Health Sciences is to determine those agents in the general environment which have a deleterious effect upon man's health. This is in contrast to the mission of the National Institute for Occupational Safety and Health which is to develop criteria for standards to protect the working population of the United States from the multitude of health and safety hazards to which it is exposed.

Therefore, the work of the National Institute of Environmental Health Sciences, which bears on the occupational environment, is concerned with the investigation of those substances which have potential for becoming a general environmental health hazard.

A total of approximately $815,000 was obligated during the past year on research (center, project, and individual) projects related directly to the work environment. These figures do not include work of the effects of effluents from industry on the general population. The work was primarily in the areas of etiology and pathogenesis, including epidemiology.

Mr. FLOOD. When you identify a hazardous substance what do you do about it? Give us a couple of examples.

Dr. RALL. It is generally a long process between the time you say this might be hazardous—there is first a suspicion, and then perhaps weeks or months or even years later———

Mr. FLOOD. No; look what I have. There it is. What do you do?

Dr. RALL. There are two things you do. You make copies of your results and mail them out to your colleagues in the other agencies who may be involved in this. The other thing you do is you telephone them. This is the most effective way I know of for quickly involving those people who ought to know.

Some of the examples, the problem with asbestos in the Duluth water supply. The toxicology coordinating committee for Health, Education, and Welfare quickly assembled those people in the Department who were involved. The National Cancer Institute, the National Institute of Occupational Safety and Health, the Center for Disease Control, and our Institute met immediately to try to determine what we knew about the hazard of low concentrations of asbestiform fibers in drinking water, how we could get more information on this problem. We each drew on our own area of expertise to determine the extent to which we could help the other.

For instance, the epidemiology program in the Cancer Institute is very strong in identifying cancer mortality in various counties. They were able to identify counties in and around Duluth, and look for cancer mortality. It turned out at the moment it doesn't look like there are any differences, but it is too early to tell.

NIOSH is very good at measuring fibers in the air, and they quickly began to look at this problem. The committee then recommended that we develop the philosophy of a protocol to study the oral toxicity of asbestos.

Asbestos has been around for a long time, but most people have viewed it only as a danger from inhalation, by breathing it in. This is the common form of asbestos damage.

Oral intake of asbestos has really not been studied very much. The committee has put together a very important protocol to look at the long-term hazards of oral asbestos. This is a protocol which will probably cost between $1½ million and $2 million a year to complete and take probably 3 years.

Oral asbestos is so widely distributed not only in Duluth where Lake Superior water contains asbestos-forming fibers, but much of the water supply of the United States, particularly in the Southwest, goes through concrete pipes which contain asbestos. We simply do not know how much of the asbestos gets into the water and how hazardous it is.

ENVIRONMENTAL HEALTH SCIENCES CENTERS

Mr. Flood. How many of the Environmental Health Science Centers are you supporting in 1974, and how many are you going to support in 1975?

Dr. Rall. We are currently supporting six. We are expecting to add one in 1975.

Mr. Flood. In your justifications, you said each center would concentrate its efforts on more and more areas vital to the occupational hazards. I know that Dr. Selikoff at Mount Sinai Center is working primarily, as you indicated, on asbestos.

What has he learned about the asbestos problem?

Dr. Rall. At Duluth or in general?

Mr. Flood. What is he doing at Mount Sinai?

Dr. Rall. He is trying to correlate the heavy occupational exposures which we have really quite good data for, to the later, less intense environmental exposures which we have very poor data for. This has been one of his major efforts.

He also has been in the forefront of attempts to measure asbestos in the food, in the water, and in body tissue. The identification of these very fine fibers is a very difficult process. They are approximately one-millionth of a millimeter thick, and six-millionths or eight-millionths of a millimeter long. They are very difficult to identify in food, in the water supply, or in human tissue at autopsy. This has been a major effort on his part.

Mr. Flood. Give us a list of these centers now and a brief description of what kind of work is being conducted at each center.

Dr. Rall. In addition to Mount Sinai, there is a center at Harvard University under Dr. Whittenberger, which again is interested in the connection with occupational and environmental health. They are interested in other problems such as sulfur oxides in some of the New England paper factory towns. They are interested in problems of the toxicology of a variety of occupational and environmental chemicals. They have one of the best epidemiology departments in the country.

Mr. Flood. Does anybody take a look at flour mills?

Dr. Rall. I am just trying to think. I haven't read of any studies on flour mills. I suspect they are quite dusty, and dust in itself can cause problems.

Mr. Flood. Textiles?

Dr. **Rall.** In textiles, cotton weaving can cause byssinosis. Byssinosis, cotton dust fever, is a fairly severe occupational disease itself. We have research going on in byssinosis. This is a problem particularly in those States which have a substantial fiber industry, such as North Carolina.

Another center is at the University of Cincinnati under Dr. Raymond Suskind. This is the center that will be looking at anthracite coal very soon and have been worried about this problem of the toxic components of a variety of different coals. They are interested in the toxicity of some of the heavy metals, lead and mercury.

They also have a close tie to some of the occupational problems, since they are located quite near the research laboratories of NIOSH.

At Oregon State University in Corvallis under Dr. Freed, there is a center which is more concerned with agricultural products, pesticides, and so forth which eventually find their way into the human food chain and exposure to man.

Another center is at New York University, Dr. Norton Nelson. This center is the one that first showed the incredible carcinogenicity of the halo ethers. This is really a major research finding. About 3,000 workers have been exposed, and it is expected there will be some deaths resulting from that exposure.

HALO ETHERS

Mr. **Flood.** What is the significance of the term "halo ethers"?

Dr. **Rall.** Halo means——

Mr. **Flood.** It is sort of a frightening phrase.

Dr. **Rall.** It is a generic word for a group of atoms, chlorine, bromine, iodine and fluorine. By identifying these we have probably protected many thousands of workers in the future.

The problem now is that the effluents from some of these plants contain halo ethers which are not destroyed in the environment and be taken up in the water supply of towns that are downstream.

POLYCHLORINATED BIPHENYLS (PCB'S)

Mr. **Flood.** You mentioned briefly in your statement the substance PCB's. Will you translate that for the record?

Dr. **Rall.** These are polychlorinated biphenyls.

Mr. **Flood.** We have talked about that for a couple of years.

Dr. **Rall.** We have indeed.

Mr. **Flood.** Again you have it in your justification, properly. Last year you told us you would be working with Japanese scientists to learn much more about this substance. Have you learned anything new?

Dr. **Rall.** We have been less successful than we hoped we would be. The Japanese as you know had a very severe epidemic of PCB poisoning some years ago and we have not been able to get as much information as we would like.

Mr. **Flood.** You told us about that and I was wondering.

Dr. **Rall.** We have been very disappointed.

Mr. **Flood.** In what, their cooperation or the study?

Dr. **Rall.** The difficulty is in getting cooperation to find out exactly what happened to this group of people exposed to PCB's.

FOOD TOXICITY

Mr. **Flood.** How much research are you supporting to determine the toxicity of synthetic substances in food? You can imagine what an audience you can get for that discussion. Have any synthetic substances actually been removed from the market in the past year as a result of what you have done in your research?

Dr. **Rall.** No.

Mr. **Flood.** Tell us first how much you are doing in this area? How much research are you supporting in that very important area?

Dr. **Rall.** I will have to look that up. Now that we have our new budget mechanisms we don't have some of the information as nicely available as we used to. Between $250,000 and $300,000 in this general area of food additives and adulterants.

Mr. **Flood.** Is there anything in the last year you have specifically removed?

Dr. **Rall.** No, I don't think anything has been removed from the food in the last year.

One interesting problem is the synthetic substance in food but it is synthesized by the food itself. This is research coming out of our last center at Vanderbilt University, Dr. Neal, where they have been looking at some toxicants from the sweet potato. They have the general name of ipomeanol, a name which I can hardly pronounce.

These are formed by the good part of the sweet potato underneath the bruise. In other words, if you take a sweet potato and bruise it, underneath the damaged part there will be, as a part of the synthetic activity of the sweet potato tissue itself, a group of compounds that are toxic to mammals.

Mr. **Flood.** That is not peculiar to the sweet potato is it?

Dr. **Rall.** No, a number of other similar vegetables about do this. But it is found particularly in sweet potatoes. These can cause pulmonary and kidney diseases. We are fairly concerned about them.

CLEARING HOUSE FOR INTERNATIONAL EXCHANGE OF ENVIRONMENTAL PROBLEM

Mr. **Flood.** We have been told that your Institute has become a clearing house for international exchange on the environmental science problems. Is this correct and how do you go about fulfilling this role?

Dr. **Rall.** We are beginning to, and this is very important, just to give an example of a couple of years ago, there is the red dye, F.D. & C. red No. 2 which we are exposed to in a whole variety of ways which was first reported by our Soviet colleagues some years ago to be teratogenic. This was before our U.S.-U.S.S.R. program was going. It took a long time for that information to get to the United States, to be confirmed, and FDA has just been taking action in the fairly recent past. We hope in the future the channels of communication will be such that we can move much faster indeed.

FACILITIES IN NORTH CAROLINA

Mr. **Flood.** Last year you told us that Mr. Miller wrote a letter to OMB requesting the release of funds appropriated to planning construction of facilities at your Institute. Has Mr. Miller received a reply to that letter?

Dr. Rall. Yes, a very nice reply. I remember last year I said it was a nice letter and I am happy to say OMB sent a nice reply back and they released the funds.

Mr. Flood. Is the planning for the facility under way?

Dr. Rall. Yes. We now have hired our architects and engineers and the planning began about 6 or 8 weeks ago and they have a 20-month deadline.

Mr. Flood. What is the nature of the facility?

Dr. Rall. This will be a laboratory complex with proposal of about 310,000 gross square feet. This will be our main laboratory facility.

INTRAMURAL RESEARCH PERSONNEL

Mr. Flood. Your budget shows 197 positions assigned to intramural and clinical research. How many of these positions are assigned to each one of the six branches you mentioned in your justifications on page 165. How many of these jobs are assigned to each one of those?

Dr. Rall. I will supply that.

[The information follows:]

The positions are assigned to each of the six branches as follows: Environmental biology and chemistry, 56; environmental biometry, 7; environmental biophysics, 12; environmental mutagenesis, 20; environmental pharmacology, 26; environmental toxicology, 32.

The remaining positions are research support positions involving such activities as administrative services, glassware, research and engineering services, and library services.

Mr. Flood. Are all of these people working at the laboratories in North Carolina?

Dr. Rall. Yes, indeed. We have one permanent full-time person on our staff in Bethesda.

INTRAMURAL RESEARCH

Mr. Flood. You indicate that you are requesting a program increase of $868,000 for intramural research. But I notice that you are not asking for any jobs. How do you expect to expand the intramural research program without an increase in positions to make it work? How do you do that?

Dr. Rall. One of the major reasons for the increased dollars is because of the increased costs of doing scientific research. And the money we will get will allow us to keep current with the new technology and the new methodology.

Mr. Flood. Is this just inflation?

Dr. Rall. Inflation in the economic sense as well as the more sophisticated sorts of studies requiring more sophisticated equipment. Without an increase in positions we will not be able to do an increased amount of research however.

Mr. Flood. That is what I asked you. You are not asking for any increase in positions, you are asking for $868,000 to produce so and so but no new positions.

Dr. Rall. That is right.

Mr. Flood. You mean you wave dollars instead of a wand?

Dr. Rall. Having the dollars will let us do more sophisticated and better research.

Mr. Flood. Take a look at page 157 and for the record give us a breakdown of the increase of $901,000 and tell us how that money will be used.

[The information follows:]

The increase for intramural laboratory and clinical research of $955,000 contains $54,000 for increased personnel costs and $901,000 for other expenses. The $868,000 is included as a program increase. The remaining amount is for net mandatory increases. The program increase will provide strengthened support for the areas of environmental mutagenesis and reproductive toxicology and etiology of environmental diseases and disorders. These new research areas require increasingly sophisticated supporting technology and equipment. The increase will permit modest development in these areas.

RECRUITING

Mr. Flood. Do you have any difficulty in your shop recruiting and retaining research personnel?

Dr. Rall. We have not had any trouble recruiting or retaining research personnel.

Mr. Flood. Salaries are a problem?

Dr. Rall. Salaries are a problem at the higher level. I want to come back to that. We are a young institute and the average age of our scientists is very young and they are very excited about what we are doing.

Mr. Flood. When was your institute born?

Dr. Rall. 1967. We have had a very serious problem trying to hire an associate director. We have a man in mind who is a board certified pathologist currently on the faculty of a university with particular expertise in the area of lead toxicity. He tentatively accepted the job at a salary reduction but then when the $35,000 limit was not increased he felt that for his own financial future he had to go out and look at other jobs. He is currently making up his mind. He is considering another university position which would pay him $50,000.

Mr. Flood. Do you find being located away from Washington is an advantage or disadvantage from the standpoint of attracting and retaining personnel?

Dr. Rall. An advantage. A climate with three superb universities is very attractive.

Mr. Flood. Would you rather be in Bethesda?

Dr. Rall. No, I wouldn't. I would rather be down there. However, I personally get a little tired of riding the airplane back and forth.

RESEARCH EXAMPLES

Mr. Flood. In your statement you say "The scientific base of knowledge developed by NIEHS is essential to rational and effective regulatory action, most importantly the development of effective preventive measures."

What about an example or two of cases where your research has actually led to regulatory action or preventive measures.

Dr. Rall. The one example I gave which is the most clearcut are the halo ethers. We have literally prevented many, many deaths from bronchocarcinoma. In our studies of nitrilotriacetic acid (NTA), the synthetic detergent, we are still not certain but it is very possible, some of our studies have made it such, that this agent is not safe to use. We are not sure. We are still working on it. The early studies done when the Institute was really in its infancy on the carcinogenesis of a variety of industrial compounds and pesticides have certainly cut down the burden of environmental carcinogens in our environment.

A most dramatic recent example is one of our grantees who was able to develop a method for this extremely potent compound tetrachlorodibeno-p-dioxin known as TCDD. This appears only as a contaminant, but it contaminates such things as pentachlorophenol you put on fence posts and wood to prevent rotting, and a herbicide 2,4,5-T. The beautiful new method these scientists developed allows us to detect fantastic small quantities of this. But this is such a toxic agent you need to detect those small quantities to monitor.

These researchers for instance have found significant amounts of this contaminant in the fish and shrimp caught in South Vietnamese waters, and we are now trying to investigate whether or not there are other examples of TCDD contamination of such seafoods.

Mr. FLOOD. Mr. Michel.

Mr. MICHEL. Thank you, Mr. Chairman. I apologize for my tardiness today. I understand we do have some visiting dignitaries in the hearing room you acknowledged at the beginning of the meeting. I too want to acknowledge their presence, speaking for the minority.

I say to our friends from the Soviet Union if they have had an opportunity to attend a hearing in a legislative committee they would have undoubtedly experienced much more partisanship than they do in this appropriation committee hearing where Democrats and Republicans show very little of their partisanship. We submerge it in the interest of trying to get along amicably with one another and see how many dollars we can save for the taxpayer back home and still give them all of the goodies of life.

OCCUPATIONAL DISEASES

Dr. Rall, last year this committee heard testimony from Labor witnesses about what they termed a lack of serious attention to occupational diseases and criticism of the budget for your Institute as not large enough to deal with the problem.

Could such charges be leveled against your program in your budget this year with any validity?

Dr. RALL. As an Institute Director you always want to have enough money to do the very best job you can. Yes, if we had more money we could do a better job. I don't think there is any question about that. Let me give you an example of some of the problems we face.

POLYVINYL CHLORIDE

I think you are probably all aware of the developing occupational problem with the manufacture of polyvinyl chloride. Polyvinyl chloride is one of the most popular plastics in the country today. There are 6 billion pounds a year made. An incredible amount of this plastic.

A few months ago in a Louisville, Ky., plant that makes polyvinyl chloride there was first discovered about four workers with a very unusual liver cancer memanogeosarcoma. This riveted the attention of all of us involved in environmental and occupational health. It has subsequently been developed there are many more cases of this rare tumor due to polyvinyl chloride.

There are some experiments in progress in Italy which clearly show that rather modest levels by inhalation cause a similar tumor in rats. So it looks like the vinyl chloride, the monomer before you polymerize into the polymer, the plastic, is a causative factor. This I think will be a major problem in the next few years.

I bring this up because we were aware of the general problem of the potential toxicity of these reactive monomers 3 or 4 years ago and we simply didn't have the resources to devote to this new area and did not feel we properly could divert resources from other important programs to start a new program on vinyl chloride toxicity.

Mr. MICHEL. Would that be your No. 1 priority if you were to have additional funds available?

Dr. RALL I think my No. 1 priority—we know now that vinyl chloride is a problem——

Mr. FLOOD. Those four liver cases you mentioned were fatalities weren't they?

Dr. RALL. Yes. They were autopsies.

Mr. SMITH. Did those four and these additional ones that suffered work in the same part of the factory?

Dr. RALL. Yes.

Mr. SMITH. What part of the factory?

Dr. RALL. Most of the cases so far were those men who went into the vats after the polyvinyl chloride was made and cleaned the vats literally by chipping it out. They were very heavily exposed. Dr. Selikoff and the scientists from NIOSH are now looking at broad segments of workers who are involved in PVC manufacture.

This is a problem we know about.

My first priority I think is to try to anticipate problems, to try to find out ahead of time before 30,000 or 40,000 people are exposed or before great segments of the population are exposed. To do this you need to have the freedom to move resources quickly and have ample resources so you can study many of these ideas.

A number of them will turn out to be no problem at all, but that is but that is fine, that is good. But you have to be able to explore the vinyl chloride and vinyl chloride toluidinechloride, which is a similar one we haven't begun to look at yet, a variety of the toxic chemicals which first exposes workers and then get out into the general environment broadly.

Mr. SMITH. And once exposed your obligation is really fulfilled and it is up to other agencies of the Government or the private sector to implement and put into better practice your findings to eliminate this in the future.

Dr. RALL. Right. It is up to us to understand the mechanism of action of the compound and how it impacts on man. The control of the substance falls to the regulatory agencies.

Mr. MICHEL. Last year we discussed your work on cyclamates and the ongoing studies you were conducting with monkeys and saccharin and monosodium glutamate and caffeine. Are these projects still underway? Can you report something about them?

Dr. RALL. Yes, indeed. The studies are not completed but they are approaching completion. But it is important to note that these issues are not dead issues, because about 3 months ago Abbott laboratories petitioned the FDA to allow cyclamates back on the market because the evidence they had accumulated suggested that the original studies which showed bladder tumors could not or were not replicated by new studies. So the ongoing experiments we have will be of increasing importance because they will help make the final decision as to whether cyclamate goes back on the market and saccharin comes off. This is a possibility.

DIETHYLSTILBESTROL (DES)

Mr. MICHEL. How about diethylstilbestrol which, of course, we did feed to cattle to help in their fattening process, and it was taken off the market. Isn't there a similar suit pending there?

Dr. RALL. It is my impression that the order banning diethylstilbestrol was turned aside by a procedural matter suit.

Mr. MICHEL. I am not altogether sure.

Dr. RALL. This was procedural, not scientific.

Mr. MICHEL. I am sorry I don't have the information here specifically, but I remember getting some information from the National Institutes of Health for a speech I was giving back home and, in reading through some materials, I was rather surprised to learn at the same time we were taking diethylstilbestrol off the market for feeding cattle it was being used in the treatment of children afflicted with muscular dystrophy in some research activity. I will have my staffman get that from the office because I wanted to use it in the course of the hearing to really find out whether again this is one of these instances where there's a question if the right hand knows what the left hand is doing.

Dr. RALL. I don't know the specific instance with diethylstilbestrol and muscular dystrophy.

Mr. SMITH. Like in the pill.

Dr. RALL. Not quite. It is a related but different chemical. If you are treating a disease like muscular dystrophy, a fatal disease in a reasonably short time, I think you are justified in using chemicals potentially hazardous and which you would not want the entire population exposed to.

ENVIRONMENTAL HEALTH SCIENCES CENTERS

Mr. MICHEL. You said in answer to the chairman's question that you were going to have one new environmental health center at a cost of $1,100,000. What would be done there that isn't being done elsewhere? Is it just an expansion of what is being done in the others or is there a specific area in which you envision something we are not doing now?

Dr. RALL. The center would primarily be for heavy metal toxicity. We think there are many reasons why that is going to be increasingly important. One of the problems with an increased use of coal is that many heavy metals are in coal and can't be removed by any prewashing techniques, and may end up as general environmental contaminants. So we look forward to an increased need for knowledge about heavy metal toxicity, environmental distribution, and so forth.

Mr. MICHEL. Is this the only effort in your shop in this area?

Dr. RALL. No. We have many efforts in heavy metals at Dr. Suskind's center in Cincinnati and a variety of others. We are supporting a number of research projects as one at the University of Rochester.

Mr. MICHEL. You heard the chairman many times make mention of his coming from a very important coal producing area of the country. We in Illinois have large reserves too and more and more attention is being given to that. It would seem to me that in that particular area we would want to be giving emphasis to it on an increasing scale. We should expedite that kind of research, because time is of the essence.

In your discussion of AF–2 on pages 3 and 4 of your statement you say the problems associated with the use of this compound in Japan points up the need to develop more precise and rapid methods to screen chemicals prior to their release and better methods to monitor the population and evaluate the extent of genetic damage produced as a result of accidental exposure to the mutagens.

Could you be more specific as to what you specifically have in mind, what kind of operation it would take to do what you think would be adequate?

MUTAGENIC TEST SYSTEMS

Dr. RALL. The two problems are, first, among the very, very many chemicals in our environment how do you identify those few that are likely to be mutagenic. The current test methods, first of all, are very time consuming and require quite a few animals and a lot of manipulation. Thus, they are expensive to do and inhibit the testing of new compounds.

What we are trying to develop are test systems using, first, microbial agents or other one-celled organisms; and, second, some sort of mammalian or human cell in tissue culture. This could be done rapidly and cover a number of compounds and move on to a sort of sequential system in the more complex mammalian systems.

Our geneticists are devising a number of very elegant methods of looking at serum enzymes controlled by genetic processes and which vary as a mutagenic event has happened.

The next problem is how do you tell in man whether a mutagenic event has occurred. By the same token we are looking for cultures of human cells to see if we can detect differences in enzyme patterns in human cells after a mutagenic event, whether some of the serum protein, the protein in the blood, have a different structure after a mutagenic event.

What we look forward to is the ability to take a small amount of blood, perhaps scrape off a little of the bucal mucosi to get some cells that are living, analyze the blood, grow the cells, and find out whether a mutagenic event has happened. It is a very difficult process I might say.

Mr. MICHEL. In your discussion of reproductive toxicology, have you found that thalidomide has caused the same effect in rats and mice and rabbits as was caused in human beings when it was used?

Dr. RALL. This has been one of the most disturbing things about the teratology testing systems that we know. Thalidomide would probably pass all our current teratology test systems. It would pass. It would not show up as a teragen. You have to go to great lengths in the rabbit or use the monkey to show thalidomide as teratogenic. If you do that, you get exactly the same syndrome you see in man. This is why we feel we need more research on developing better test systems. If the current test systems miss what is the major teragen I don't think they are really very good.

Dr. STONE. The same thing applies to carcinogens. Human beings often react differently from the animals and might show a carcinogenic effect when animals do not, or vice versa. It is an extremely difficult problem.

AEROSOL SPRAYS

Mr. MICHEL. Have your studies of the propellant gases and solvents in aerosol sprays you mention on page 7 of your statement, led to any tentative conclusions about safety of aerosol sprays?

Dr. RALL. The sort of worries we have are not with the occasional use in a well-ventilated room of the typical spray. What we are concerned about is a woman in a small bathroom without ventilation, spraying her hair for 60 seconds instead of just a couple of seconds. We are concerned with the cartiotoxicity of these agents. We are concerned about some of the freons which are used in a hospital setting to freeze tissues because there is some evidence developing from our center at Harvard University that the technicians or the pathologists can inhale these freon fumes in a confined state, and this may lead to cardiac irregularities.

These products, I am sure, are safe if they are used in a well-ventilated place to a modest extent. But if you use them too long or in a closed room, we are worried.

Mr. MICHEL. Are you in any position yet to make any recommendations to the regulatory agencies on aerosol sprays?

Dr. RALL. We are not making any formal recommendations. We are talking to our friend at the Consumer Product Safety Commission. One of our toxicologists testified at their hearing on the safety of aerosol products, and we are in constant communication with them about it.

Mr. MICHEL. Evidently my man Friday did get this out of the file, and there is a statement here under crippling diseases of children: "The research team had been administering doses of DES to muscular dystrophy children. This synthetic hormone was found to significantly reduce the blood levels of two crucial enzymes prevalent in muscular dystrophy children." That is what struck my attention.

Dr. STONE. I am confident they are aware of the problems.

Mr. MICHEL. I think your opening statement said to the effect that short-term or small dosages in experimental cases might well, if they open up some new avenues, be justifiable if not used over a long term.

That is all.

Mr. FLOOD. Mr. Smith.

MONOSODIUM GLUTAMATE

Mr. SMITH. I mentioned monosodium glutamate.

Dr. RALL. Yes.

Mr. SMITH. That, of course, is sold in the grocery store under a brand name. It says right on it, however, that is all it is. What else can you tell us about this?

I happen to be a victim of it. I went to a restaurant about 4 or 5 months ago, and that night I had the worst headache I have ever had in my life. I asked the doctor about it, and he tied it down to the hamburger I had, which tasted good. It really tasted great. It was a great big hamburger, and I ate it. He said the restaurant put too much monosodium glutamate on it.

What can you tell us about this?

Dr. Rall. There are two problems with the toxicity of monosodium glutamate. The one that you describe, which is now known as the Chinese restaurant syndrome because Chinese cooking uses enormous quantities of monosodium glutamate, and the very typical picture is the man who goes out and has a Chinese dinner and ends up with a terrible headache and feels somewhat ill and it goes away in a few hours. This can be reproduced by giving you a couple of grams of monosodium glutamate. It is perfectly harmless. It is not very much fun.

The other more serious problem relates to the susceptibility of very young animals to high doses of monosodium glutamate. If newborn mice and rhesus monkeys are given a dose of 1 or 2 grams of monosodium glutamate, they get permanent neurological damage.

This sort of research led to the removal, a voluntary removal, of MSG from all of baby food because it isn't necessary for the babies. To what extent this is a major problem, or one that simple removal of MSG from baby food will take care of, is not certain. That is the one we are worried about.

Mr. Smith. Is enough being done to warn restaurants and those that use it what will happen if you use too much of it?

Dr. Rall. A sort of warning on the bottom of the menu?

Mr. Smith. I don't know how you would do it.

Dr. Rall. I don't know quite how you would do it either. However, this is a general public health problem which is usually the responsibility of State and local health departments.

Mr. Smith. I wonder if the cooks in the restaurant know enough to use that stuff rather sparingly?

Dr. Rall. I don't know how widely known it is in the public. Certainly, among the medical profession, the Chinese restaurant syndrome is well known.

Mr. Smith. Apparently it reaches a lot of restaurants that don't have Chinese food.

Dr. Rall. Yes, indeed.

Mr. Smith. That is all.

Mr. Flood. Mr. Patten.

COMMUNICATION

Mr. Patten. Doctor, your field is research, but Mr. Smith pointed up the difficulty of communication. When you tell of your experience with Japan, after a 10-year period, it makes one wonder.

Let's take our guests here today and all the work they do. How would you communicate with the Russians—send them a letter?

Dr. Rall. We have a telegraph machine in our Department of Health, Education, and Welfare, which is linked directly to their Ministry of Health. We can get a message within 10 or 15 minutes to the Ministry of Health of the Soviet Union.

Mr. Patten. Does it amount to anything?

Dr. RALL. We haven't yet used the Telex for communication of research funding but have found it useful for coordinating our health agreement activities with those of our Soviet colleagues.

Mr. PATTEN. You don't have the same equipment with Japan then?

Dr. RALL. We don't have as good a relationship because of internal problems in Japan.

VINYL CHLORIDE

Mr. PATTEN. A couple of days before I read about the vinyl chloride and cancer, an old friend running a plastic plant who was complaining he was only getting 300 pounds a week and needed 600 pounds. I got down here and picked up the telephone and called the supplier, and apparently his situation eased a little bit.

You referred to four cases. Is this in the industry the total number of cases?

Dr. RALL. The four cases were the original four that got attention.

Mr. PATTEN. Do we know in how many deaths from cancer?

Dr. RALL. No; we are looking. The people from National Institute for Occupational Safety and Health, the other involved people, the companies, Dr. Selikoff's group are searching through the records, and I am sure it will be much more than four. I think as of now there are about 12 or 15.

Mr. PATTEN. Would my friend who is using 600 pounds a week know that the fellows who clean out the vats are especially exposed?

Dr. RALL. I don't know. I gather there is a new temporary standard put out by OSHA in the Department of Labor to hold the exposure down to 50 parts per million, which may not be perfectly safe but certainly it is much, much better than it was before. So he might well be aware of that.

Mr. PATTEN. Would you believe I have many plants in the area that use vinyl chloride.

Dr. RALL. How many of those manufacture PVC or how many buy PVC and use it?

Mr. PATTEN. They buy it.

Dr. RALL. They are not in such bad shape. It is the plant that manufactures it that takes the vinyl chloride monymer, react it and form the plastic which they then ship to various plants.

Mr. PATTEN. Of course it is out of your line, but when I was 16 years old I was a clerk and had to fill out an accident report. I put down lead poisoning. I called to the head office and they changed that to a cold. The nurse said you would be surprised what would happen to our compensation rate because we would have to report lead poisoning to the State.

I went up to the house and saw the fellow and his bowels hadn't moved in 25 days, blue lips, dropsy, and he died. And the death certificate by the undertaker said lead poisoning. I was asked to put down he had a little cold.

Dr. RALL. I am not an expert, but the Occupational Safety and Health Act of 1972 goes a long way to doing this. It really has changed the relationship enormously.

Mr. PATTEN. We have a new program and in my book it is not off the ground.

Dr. RALL. I think at least the sort of example you describe would be very difficult to do now.

Mr. SMITH. Will the gentleman yield?

Mr. PATTEN. Yes.

Mr. SMITH. The gentleman from New Jersey asked about communications. I was wondering, in expanding on that, to what extent has the World Health Organization headquarters in Geneva helped this communication, or have they?

Dr. RALL. Their environmental health program in the past was not a very strong one. Fortunately 2 or 3 years ago the very able and energetic Dr. Dietrich came onboard to head their environmental health program. I think he is moving in the right direction, increasing communications between the member countries, interchanging national reviews of problems, and convening meetings at appropriate times. I think this is a very good omen. In addition a member of my staff has been working in Geneva for the World Health Organization over the past year.

NOISE POLLUTION

Mr. PATTEN. You indicated in your justification that on noise pollution we have done very little. I saw a picture of the New Jersey State Trooper with some equipment on the highway and they were going to test the noise factor of trucks. The article said under some new laws we have probably 15 percent of the trucks would be pulled over and would receive a ticket. We have a lot of complaints from our people especially about the airplanes. We have had them since I have been in Congress. Frankly, as far as what we know about noise pollution or the effects around the neighborhood, believe me there is not much in my file from the scientific viewpoint or research on noise pollution. As far as I am concerned we are just a little bit further ahead than just merely mentioning the problem or the study. I don't think we have done much with it.

Dr. RALL. The Federal budget for noise research look fairly impressive if you just look at it. The total is in the order of $100 million and that sounds great. But then when you begin to look at how that is divided up, only about 2 or 3 million is involved on human health effects of noise, and all of the rest is for technical assistance to make existing noisy areas more quiet. I am agreeing with you 100 percent that we make a lot of noise but we don't do much about it in terms of finding out what the effects are, to what extent is it damaging to man's health.

We have a small noise program, something in the order of $350,000 this year. We think it is a very important area, but we are investing all we can afford at the moment.

Mr. MICHEL. If the gentleman will yield, this last week a number of representatives from one of the largest industries in the country, which is located in my district were down here with regard to the development of their new truck engine that would have to meet these new noise standards. Some of the tires have already been eliminated for on-highway use in view of the new restrictions. So there are some economic factors involved here, too, that you have to take over an extended period of time rather than summarily having the Government step in and tomorrow close down some basic industry for failing to meet a standard. It is a long range thing.

Dr. RALL. This other problem that worries me very much is what you brought up—that in the noise area if we conform to the standards that EPA and OSHA are in the process of promulgating, this will cost literally billions of dollars. But I don't think it makes economic sense to put only a couple of million dollars a year into human health effects noise research when those results are going to force an expenditure of billions of dollars. I don't think that is good economics.

Mr. Patten. I am impressed by the scope of the work that might be ahead of us in your Department because I am under the impression that in my State there are about 500,000 people employed in the chemical industry. It is more a case of hush hush and keep your mouth shut with State departments and Federal agencies. I don't think we face up to the problem for fear of loss of production and loss of jobs. I know in the chemical industry over a 50-year period we could have gathered some very interesting data.

You mentioned things like coal, iron, copper, lead, zinc. Those of us who have some experience in plants of that type know full well there are occupational hazards involved. I think our whole policy is to brush it under the rug.

Good luck to you.

Dr. Rall. Thank you.

Mr. Flood. Mr. Obey.

Mr. Obey. Thank you, Mr. Chairman.

ENERGY

Doctor, I have been told that—I think I am right on this—that you are heading up a review of the impact that the energy crisis has had on the conduct of biomedical research and on almost everything from the availability of plastic cages for research animals to possible reallocation of manpower. Am I correct on that?

Dr. Rall. Well, not quite. We have been very concerned about the human health implications of the energy crisis first, and second the search for new forms of energy.

NIEHS organized a small meeting in early February where we got the various Federal agencies who were clearly involved in this with representatives of the Ford energy policy study and the Office of Management and Budget to just try to think about what the problems are going to be.

I would like to review a few of these concerns about the human health hazards of new energy sources because I think here is the time when we can do a little forward planning.

The administration's proposal is to develop new energy sources over the next 10 or 20 years. We now have time to look at the human health implications of these different kinds of energy sources and to begin making some choices which will provide the least damage to human health.

The United States is fortunate in that it has a variety of energy resources and it seems likely we can make some choices. We don't have to take everything.

FOSSIL FUELS

The sort of areas we are concerned about are first the fossil fuels. We do know that there are many problems with mining coal. There are problems with the few plants that have been involved in coal gasification and oil shale recovery and tar sand recovery which have yielded workers that have had skin cancer in a short period of time.

There is good evidence that the complex organic polycyclic aromatics from coal, from oil shale, and tar sand are quite carcinogenic indeed.

I think this is a problem we must look at before we get too far down the road. To what extent this will be more than an occupational hazard is very hard to tell. There will certainly be some environmental discharge and distribution of these compounds.

To what extent they are mutagenic and teratogenic in addition to being carcinogenic we don't know. So this is a major problem.

The effluent from burning coal brings us back to the old problem of particulates, sulfur oxides, nitrogen oxides.

The other problem is that of heavy metals. About half of the mercury in our environment comes from burning coal. The mercury in the coal is volatilized and goes out the stack. We are worried about other heavy metals.

In the fossil fuel area, in the supertanker business, there are some very preliminary indications that oil spills may be more toxic to marine life than had been realized, and this is an area which is going to be very, very important.

The next option is the nuclear option, and I won't discuss this. I think the problems of radioactivity and radioactive nuclides have been well surfaced. We are not sure they have been well studied.

Some of the fascinating new methods of developing energy, such as geothermal, which utilizes the hot water deep in the ground, again you run into the problem of heavy metals. Arsenic, lead, cadmium are in these waters from deep within the earth and can contaminate. Also radioactive nuclides, the thorium series and so forth may be in these waters.

You get then into some of the other more esoteric forms. We are beginning to develop them, fuel cells, photovoltic cells and so forth, with compounds which just haven't been used before. And we obviously must know more about the toxicity of these.

INSULATION MATERIALS

If you take the other concept, that, in addition to developing new fuel supplies, we must be much better at conservation, you begin to get back into the asbestos problem. This means greater use of asbestos as an insulating material and increased use of rock wool. We know very little about the toxicity of rock-wool fibers. Also fiberglass is the other major insulating material.

We do know the new fine fiberglass fibers may have the same toxicity as asbestos. So it seems to me we have a major new environmental health problem to look at in the new energy program.

Mr. Obey. You mentioned rock wool and fiberglass. What would be your estimate of what amounts of money are being spent to research the toxicity of those two items?

Dr. Rall. In the entire United States I would suspect there is less than $100,000 on rock wool and less than $500,000 on fiberglass.

Mr. Obey. That would be broken down how much between Government versus private or universities?

Dr. RALL. I suspect that is mostly all Government, but I don't really know.

Mr. OBEY. If one were trying to put together what the potential health costs would be of adopting the new administration recommendations, relaxing clean air standards, conversion of coal and all of the other items in that recommendation, how would one go about assessing what the total impact of that recommendation would be in health terms, and how, for instance, if you were at all involved in trying to assess that, would you split up your duties with EPA for instance?

Dr. RALL. I think you should put together a team of people to look at each one of these approaches. You would first need an engineer because you have to have somebody that understands the process of what is happening. I then certainly would want somebody from NIOSH who would understand the occupational, the direct occupational implications. Next, someone from our Institute who would look at the more general human health environmental effects, and someone from an EPA-like organization who would be concerned with monitoring and standard setting.

I think it would make great sense to get groups of scientists with this sort of mixture and begin to get them to look at all of the major options that we are going to be exploring in the next 5 or 10 years.

I think by doing this we could begin to be ahead of the problem instead of always catching up as it seems we are now.

Mr. OBEY. Could you give us any indication of how much of that has been done? Are there any such teams that have been put together right now?

Dr. RALL. The Environmental Protection Agency has been charged with the responsibility for thinking about this first. There will be appointed an interagency panel from HEW, EPA, NSF AEC which should hold its first meeting soon. This committee will begin to look at this and to begin to see if this can't be done. I am not sure what EPA's approach will be.

Mr. OBEY. How long do you think it would take before we could get at least a rough outline of what we are facing?

Dr. RALL. About 6 months to get a rough outline of what the problems might be and where we should look most intensively first.

Mr. OBEY. Then it would seem to me from the standpoint of prudence Congress might do well to withhold action on those recommendations until such a team has been given time to make at least an outline evaluation of what the consequences would be. What would your judgment be on that?

Dr. RALL. The leadtime on these processes is so long that there really is time if we get the biological sciences going now. All of these new processes that we are discussing will take 5 to 10 years before they are really beyond the pilot plant stage. So there is time for it. But the biological scientists have to get going very rapidly. I hope very much we can. I shall do all I can to be sure we do.

SMOKING AND HEALTH

Mr. OBEY. On another subject, somewhat related to this, lets take the question of smoking. I used to smoke about three packs of cigarettes a day. My wife said she would marry me if I quit so I did. But I think you said last year the cancer rate for people exposed to asbestos seems to be much higher only if they smoke. Given the great difficulty we have in stopping people from smoking in this country, for a great variety of reasons, wouldn't it be productive for us to be spending a lot more than we are now to determine exactly what exposure problems, there are with occupational chemicals. You mentioned in your statement on the first page that preventive measures have clearly contributed more to maintenance and improvement of the Nation's health than the curative. I would think in terms of cost we would be far better off in testing a lot more in your shop.

Dr. Rall. I would think so.

To carry your analogy a little further it looks like both cigarette smoke and asbestos are very weak carcinogens. But if you are exposed to the two together, then you get a very high incidence.

In these oil shale plants, coal gasification plants, and so forth, it is very likely there will be significant ambient concentrations of benzpyrene. This is very likely to be another weak carcinogen which again can mix with cigarette smoke. Those workers who smoke and work in these plants may be at very high risk. If they could at least be warned ahead of time this really was a major problem, you might prevent a lot of very serious illness.

PCB'S

Mr. Obey. Let me ask something on an entirely different subject. On page 7 of your statement you refer to the ability of marine species to detoxify and/or excrete PCB's, which leads me to a question about PCB's and sharks. Is my recollection right? A few years ago weren't you doing research on drug distribution in sharks?

Dr. Rall. When I was an active bench scientist that was a sort of research I liked to do the most.

Mr. Obey. Let me ask this: As I understand, in San Francisco Bay a couple of years ago, there was an unexplained shark kill with hundreds of small sharks dying, but no other fish, no other marine life. As I understand it, that is a definite oddity in that sharks are very tough. Later it was traced possibly to PCB's. Did you know anything about that? Have any shark kills reoccurred?

Dr. Rall. No, I didn't know about that episode.

Some of my colleagues have looked at the toxicity of PCB's in small sharks in the Maine coast, and it is quite toxic. It would not surprise me if there had been a massive episode of PCB contamination so as to cause such a shark kill.

ASBESTOS

Mr. Obey. Let me go back on the problem you mentioned in the Duluth area with asbestos—which affects my district. For the benefit of the committee members here, we have had a problem in Lake Superior with a company, Reserve Mining. They have been dumping 67,000 tons of tailings a day into Lake Superior for a number of years. Recently, those tailings were discovered to contain asbestos fibers. The research team at Mount Sinai, I believe funded by you, headed by Dr. Selikoff, had gone out there and worked with them and worked with the Environmental Protection Agency on that case. I understand today the judge may decide whether or not that plant is going to be closed.

I don't really want to get into the specifics of that incident today, but let me replow some of the ground the chairman did. Evidently we know virtually nothing about the incidence of asbestos in drinking water and the health problems that creates. Is that right?

Dr. RALL. That is right. We know very little.

Mr. OBEY. You have outlined what some of your plans are for trying to find out. How much will you be spending in that specific area this year?

Dr. RALL. This year, our funding has been somewhere between $500,000 and $700,000, with about $900,000 next year.

Mr. OBEY. How much was it last year?

Dr. RALL. About $700,000.

Mr. OBEY. So there is no appreciable increase in spite of that problem?

Dr. RALL. No.

Mr. OBEY. In light of Dr. Selikoff's findings—I am just a layman, but it would seem to me the only difference between breathing asbestos fibers and absorbing them in your drinking water might be you got a different kind of cancer. Maybe that isn't true, but it would seem to me rational to expect that. In light of Dr. Selikoff's finding, it would seem to me to be awfully difficult to justify not increasing your budget for that problem. What is your response to that?

Dr. RALL. We think it is a very, very important problem, but we don't know from where to take the money.

PETROCHEMICAL INDUSTRY

Mr. OBEY. My people think it is an important problem, too. My State has no control over what Reserve Mining does, for instance, but people in Superior and other communities in northern Wisconsin drink water derived from Lake Superior.

I understand the judge is even considering in the case of Duluth and other communities, requiring that bottled water be provided.

It seems to me in that case you could certainly justify higher expenditure of funds, if not by taking it from other sources, then by increasing the overall budget.

I talked to some people from CBS News a couple of weeks ago, and I understand they are doing a series of programs on the impact on environment by the whole petrochemical industry. How much are you spending in your shop on that question?

Dr. RALL. The petrochemical industry has such broad ramifications that a significant proportion of our budget could eventually be tied back to that. Vinyl chloride comes from the petrochemical industry. Halo ethers are involved in the petrochemical industry. We think this is a major problem. Many of these compounds have toxic potential. They can cause occupational hazards; they can cause general environmental hazards as well as—and I am talking about human health hazards—in addition to despoiling the environment in the esthetic sense.

Mr. OBEY. I recognize this is sort of an open-ended question. But given the small amount of knowledge we have in that whole area, how much of an incremental leap in funds do you think your Institute could practically put to use in any one given fiscal year for studies in just that one area?

Dr. RALL. In that area, I would think something in the order of $5 million to $10 million would be very useful. The last report of the PSAC Committee on Chemicals and Health suggested that our Institute be supported more generously, and it felt we could——

Mr. OBEY. Who?

Dr. RALL. The President's Science Advisory Committee Panel on Chemicals and Health, made public about 4 or 5 months ago, suggested that we could absorb an increase of about 40 percent a year and still maintain our scientific excellence. I think that is the critical problem.

VINYL CHLORIDE

Mr. OBEY. You did indicate that OSHA has now announced the standard, or is about to announce the standard, of 50 parts per million vinyl chloride. Isn't it true that Dr. Selikoff has recommended zero parts per million exposure?

Dr. RALL. That is my understanding. My feeling is I am quite comfortable at the moment with the 50 parts per million standard. This will be so much better than what happened before. As a temporary interim standard, that doesn't bother me while we can now get our information and our data together and recommend a permanent standard that very likely will be lower.

Mr. OBEY. How long is that temporary standard likely to remain in effect?

Dr. RALL. Six months. As I understand it is limited to 6 months by law. Then you must have a permanent standard.

Mr. OBEY. Would you feel comfortable with 50 parts per million as a permanent standard?

Dr. RALL. At the moment I don't think we have enough information to make a judgment as to where the permanent standards should be. I think we should do it in the next few months.

Mr. OBEY. The reason I ask, my impression is that six B. F. Goodrich companies have already reached standards lower than that.

Dr. RALL. Ten.

Mr. OBEY. Ten?

Dr. RALL. I think it is 10. My feeling about the 50 is that it is such a good change from 500 to 50 and it is very temporary, let's live with it, and worry about where we really should put the permanent standard.

Dr. STONE. I don't think much is known yet about the effect of duration of exposure. It may be that rotating and keeping the duration of exposure low would also be helpful.

What you have brought out, it seems to me, is the enormous acceleration in increasing the complexity of the technology in our environment and that we are lagging behind in the biological investigations of its effects and dangers. We are not accelerating at the same pace in our biological investigation.

Mr. OBEY. What frightens me is, as I understand, we have about 14,000 or 15,000 chemicals in the workplace right now. We have standards only for about 450 of them. I am told between 400 and 500 new chemicals come into the workplace every year. Right now OSHA has only one criteria package in place and 15 others I think recommended by NIOSH.

Your statement says:

> The intramural research program is directed toward development of a reliable data base for use in establishing standards and devising remedial methods in a variety of populations at risk from exposure to environmental and occupational chemicals and physical factors.

It would seem to me very difficult to justify continuing of your Institute's budget at just about a level level, given the exploding nature of the whole field.

That is all, Mr. Chairman.

Mr. PATTEN. How many jobs do you think there are in the United States in certain industries where they don't allow the same person to stay more than 2 years because of what they know about the environment?

Dr. RALL. I don't know.

Mr. PATTEN. There are some.

Dr. RALL. I know there are quite a few.

Mr. OBEY. One more question, Mr. Chairman.

TRAINING GRANTS

In your testimony last year about the adequacy of training grants and research fellowships and the like, Mr. Michel asked you about the adequacy of your budget last year and you said:

> I am very concerned about this. We get letters from young people, young students, young graduates who are obviously very bright, very well motivated, very interested and who have really contributed to society through research in this field. I hope in the future we will be able to provide funds for them to do the kind of research they want to do and that they are capable of doing.

What about this year? Are you any more satisfied this year on the progress you have made versus last year?

Dr. RALL. It is still a major problem. I suppose one of the bright spots is the postdoctoral training program we have been able to initiate this year which allows the fellowships for young Ph. D.'s and M. D.'s who are interested.

We have had a very, very high response when that was announced. I think proportional to the number of vacancies we have offered we have probably gotten more responses than the other Institutes. So that will help a little bit. But it seems to me there is still an unmet need.

Dr. STONE. Mr. Chairman, this is not the year for it but in another year we would like also to talk with you about marine biomedicine which, we think, is closely related to our environmental problems. The ocean is going to be so important to us that we are anxious to take extended research programs there. But in a future year.

BASIC AND APPLIED RESEARCH

Mr. CONTE. More than most NIH Institutes, yours has a combination of basic and applied research. Does this combination raise any special problems? Have you developed any special ways of bringing together basic and applied work that might be tried in other fields?

Dr. RALL. It is our view that the appropriate combination of basic research and applied research within a single organization affords opportunities rather than problems. It makes possible the coordinated development of a base of fundamental knowledge and the application of that knowledge to specific research problems in environmental health. More, it is my experience that today's young scientists feel keenly their obligation to direct their basic research in a way that meets the long-term needs of society. My own research always included both fundamental and applied studies. I found that personally very satisfying and rewarding.

FELLOWSHIPS

Mr. CONTE. In what disciplines will you be awarding the new postdoctoral fellowships in 1975?

Dr. RALL. Primarily in the areas of environmental toxicology; environmental pathology-pathophysiology; environmental epidemiology and statistics and environmental biology.

HYDRAZINE

Mr. CONTE. What are the major products using Hydrazine? Has any warning or other action been taken yet to curb its use?

Dr. RALL. Hydrazine has several important uses; the major use is in fuel—often used in rockets. Another use is as an intermediate in the synthesis of the following important agents: Procarbazine—an experimental drug for cancer therapy, isoniazid—an antitubercular agent and, maleic hydrazide—a plant growth inhibitor used in agriculture.

The exposure to this intermediate is essentially an occupational one. Hydrazine is a recognized highly toxic chemical. Rigorous control procedures are in effect in industries using this chemical.

DECREASED AVERAGE COST

Mr. CONTE. On what basis are you predicting a decreased average cost in grants and contracts—aren't costs going up?

Dr. RALL. The projected decrease in average costs per project is based primarily on three factors: A known reduction of approximately $10,000 per project for noncompeting research grants; a reduction of approximately $1.4 million in funds for training for the support of only three fewer grants; and the effect of multiyear funding of competing research grants in fiscal year 1974 results in a higher average cost per project than projected for 1975.

EMPLOYMENT REDUCTIONS

Mr. CONTE. You show an $85,000 decrease which is the annualization of savings from 1974 employment reductions. Where were those reductions?

Dr. RALL. All of the reductions were in the Intramural Laboratory and clinical research activity.

PROGRAM REGULATIONS

Mr. CONTE. Are the Institute's comments on proposed regulations of other agencies such as FDA, made public?

Dr. RALL. While each regulatory agency may treat proposed regulations differently, the Food and Drug Administration's procedure is for the Hearing Clerk to include all comments as part of the public record. It is our understanding that the Environmental Protection Agency's procedure is essentially the same. Therefore, our comments which often are only part of the DHEW comments are in fact in the public record.

Mr. CONTE. How many scientists in the environmental health sciences have been exchanged so far under the United States-U.S.S.R. Health Agreement? In what areas are exchanges working? Put that in the record, please.

[The information follows:]

Scientists have been exchanged in each of the three problem areas of the cooperative environmental health program:

PROBLEM I

Methodological basis for the assessment of the biological effects of inhaled chemicals.

Seven American scientists have visited Soviet laboratories working on the three topic areas in this problem. Return visits by Soviet colleagues are planned for completion during this year.

PROBLEM II

Methodological basis for the assessment of the biological effects of orally introduced chemicals.

Two American scientists have visited Soviet laboratories working on the five topic areas in this problem. Two Soviet scientists have visited American laboratories.

PROBLEM III

Scientific basis for the assessment of the complex biological effects of chemicals (inhaled and introduced orally).

Two American scientists have visited Soviet laboratories working on the three topic areas in this problem. Two Soviet scientists have visited American laboratories working on this problem.

Exchanges of scientists have been completed in each of the 11 topic areas within these three problem areas.

The area of the biological effects of physical factors, particularly microwave radiation has recently been added to the cooperative program and four American scientists are scheduled to visit the Soviet Union to learn of the U.S.S.R. activities in this area in May 1974 with the return visit of Soviet scientists in the fall of 1974.

MAJOR CONFERENCES IN ENVIRONMENTAL HEALTH

Mr. CONTE. What major conferences in environmental health do you have planned for fiscal year 1975?

Dr. RALL. In late summer, 1974 we are considering a conference with the Environmental Protection Agency on the "Impact of regulatory decisions in the field of organochloride compounds." Also in August 1974 the Albany Medical College, a grantee of ours, will sponsor a conference on the "Toxicity of environmental chemicals." We do plan others but plans are not quite definite as yet. Most of these conferences are in response to urgent environmental problems and typically are planned with a very short lead time.

Mr. CONTE. Will you give some examples of how you make the results of such conferences available to the general public?

Dr. RALL. First of all the published proceedings of these meetings are widely distributed. One of the reasons for holding such conferences is to provide the public a balanced viewpoint of environmental health current problems; therefore, we specifically invite the press and particularly science reporters to attend. In general, they have done an excellent job of communicating the results of these conferences to the public. Another avenue of information distribution is our professional journal, the Environmental Health Perspectives. This journal is also available to interested citizens.

PESTICIDES

Mr. ROBINSON. You stated that you regarded it to be a major role of NIEHS "to provide a neutral ground in Government for developing scientific knowledge to be used as the bases of decisionmaking by regulatory agencies." I certainly endorse the concept, and I should like to inquire as to what you have been doing toward establishing the level of hazard, if any, in the application of pesticides in agriculture, or the entry of treated areas after application of particular pesticides.

The Environmental Protection Agency and the Occupational Safety and Health Administration of the Department of Labor have been most active in promulgating regulations in this area over the past year, with little apparent reliance on well-based scientific evidence of hazard.

Have you been working with these agencies on pesticides, or have you been doing anything independently in this area?

Dr. RALL. We are not engaged in any monitoring programs for determining pesticide levels in individual fields or treatment areas per se; however, the pesticide residues on harvested crops are regulated by the FDA and the USDA. The tolerance levels on and in foods are set by these same Government agencies. There are a number of monitoring stations which determine levels of pesticides in human blood and other samples. This program called "The community studies" program is under the aegis of the Environmental Protection Agency. We have considerable independent work on basic aspects of pesticide chemistry, toxicology, and so forth, in the following areas:

1. Pathological effects of pesticides in model and human systems.
2. Pesticide accumulation in man.
3. Modes of entry of pesticides into mammals.
4. Molecular interactions and toxicity mechanisms of pesticides.
5. Pesticide metabolism in man and other mammals.
6. Induction of pesticide metabolizing enzymes.
7. Syngerism between pesticides per se and pesticides and other environmental toxicants.

Mr. ROBINSON. Are you aware of any solid scientific evidence as to the measure of hazards related to entry of treated areas after the application of agricultural pesticides?

Dr. RALL. None, except occasional reports of intoxication of blood levels in farmworkers who apply pesticides or handle crops such as tobacco during harvesting shortly after application of pesticides. This has not been systematically studied to my knowledge, but I feel this is an important area.

AIR POLLUTION STANDARDS

Mr. ROBINSON. It has been suggested that while it is recognized that air pollution is bad for one's health, the current and projected air quality standards are much higher than required for reasonable protection of public health in most communities of the Nation, and that relaxation might well be considered in connection with the energy crisis. Would you comment on the extent to which such relaxation might be accomplished without serious danger to public health?

Mr. Rall. The setting of standards which is a statutory mandated regulatory function is based upon a foundation of scientific knowledge. In my judgment, the present standards are about right to protect the public against even minor health damage. The question of relaxing pollution standards in order to reduce the potential hazard to the public resulting from the energy shortage is not a scientific question so much as it is a public policy one. Thus it is an issue which in the final analysis must be decided by the people through their elected representatives. The responsibility of those of us in biomedical science is to work to provide the best possible scientific information for the wisest possible resolution of those public policy issues.

Mr. Flood. Thank you.

JUSTIFICATION OF THE BUDGET ESTIMATES

NATIONAL INSTITUTES OF HEALTH

National Institute of Environmental Health Sciences

Amounts Available for Obligation

	1974 Revised	1975
Appropriation	$28,879,000	$28,684,000
Amount withheld (PL 93-192)	-482,000	---
Subtotal, adjusted appropriation	28,397,000	28,684,000
Real transfer to:		
"Departmental Management" (For department-wide reduction in public affairs)	-11,000	---
Comparative transfers to:		
"Office of the Assistant Secretary for Health" (To transfer administrative support activities to the Office of the Assistant Secretary for Health)	-30,000	---
"Alcoholic, Drug Abuse, and Mental Health Administration" (For Federal Employees Alcoholic Program)	-43,000	---
"Departmental Management" (For transfer of accounting functions from the OS Working Capital Fund)	-4,000	---
Comparative transfers from:		
"National Institute of General Medical Sciences" (For decentralization of scientific evaluation grants program)	+24,000	---
"Departmental Management" (For transfer of indirect cost negotiation function to the OS Working Capital Fund)	+5,000	---
Subtotal, budget authority (base obligations)	28,338,000	28,684,000
Unobligated balance restored	+4,736,000	---
Comparative transfer of restored unobligated balance to Research Resources (For General Research Support Grants)	-372,000	---
Total obligations	32,702,000	28,684,000

Summary of Changes

1974 Estimated obligations	$32,702,000
1975 Estimated obligations	28,684,000
	-4,018,000

	1974		Change from 1974	
	Pos.	Amount	Pos.	Amount
Increases:				
A. Built-in:				
1. Within-grade pay increase	---	---	---	+$30,000
2. One extra day of pay in 1975	---	---	---	+12,000
3. Wage board pay increase	---	---	---	+8,000
4. Annualization of 1974 pay raise in 1975	---	---	---	+50,000
5. BEC rate increase	---	---	---	+2,000
6. Utility increase	---	---	---	+10,000
7. Payment to "National Institutes of Health Management Fund" for centrally furnished services	---	---	---	+63,000
Subtotal	---	---	---	+175,000
B. Program:				
1. Research grants:				
a. Noncompeting continuations	---	$6,270,000	---	+4,934,000
b. Competing	---	---	---	+1,675,000
c. Special programs	---	4,223,000	---	+1,100,000
2. Fellowships:				
a. Noncompeting continuations	---	31,000	---	+578,000
b. Competing	---	---	---	+482,000
3. Training grants:				
a. Noncompeting continuations	---	2,195,000	---	+108,000
4. Research and development contracts	---	2,000,000	---	+330,000
5. Intramural laboratory and clinical research	197	7,619,000	---	+868,000
Subtotal	---	---	---	+10,075,000
Total, increases	---	---	---	+10,250,000
Decreases:				
A. Built-in:				
1. Employment reduction	---	---	---	-85,000
B. Program:				
1. Research grants:				
a. Noncompeting completed or converted to competing status	---	---	---	-2,798,000
b. Competing completed or converted to noncompeting	---	---	---	-6,624,000
c. 1974 obligations used to fund 1975 continuations	---	---	---	-1,365,000
2. Fellowships:				
a. Noncompeting completed or converted to competing status	---	---	---	-16,000
b. Competing completed or converted to noncompeting	---	---	---	-575,000

	1974		Change from 1974	
	Pos.	Amount	Pos.	Amount
3. Training grants:				
a. Noncompeting completed or converted to competing status....................	---	---	---	-1,603,000
b. Competing completed or converted to noncompeting..	---	---	---	-1,202,000
Subtotal........	---	---	---	-14,183,000
Total, decreases........	---	---	---	-14,268,000
Total net change.......................	---	---	---	-4,018,000

Explanation of Changes

Increases:

A. Built-in--These increases would provide $30,000 for the annualization of within-grade pay increases effective in 1974; $12,000 for 1 extra day of pay in 1975, $8,000 for the Wage Board pay increase; $50,000 for the annualization of the 1974 pay increase in 1975; $2,000 for the Bureau of Employee Compensation rate increase; $10,000 for increased utilities cost, and $63,000 for payment to the National Institutes of Health Management Fund for centrally furnished services.

B. Program:

1. Research grants:

   a. The increase of $4,934,000 for 98 noncompeting research grants represents the continuation cost of "new" and competing awards resulting from grants made in 1974.

   b. The amount of $1,675,000 in competing research grants reflects: (1) $992,000 for 22 new awards; (2) $608,000 for 9 competing continuations; and (3) $75,000 for supplemental awards.

   c. The amount of $1,100,000 in special programs is for the initiation of 1 new center and the increased continuation costs of the currently active centers

2. Fellowships:

   a. The increase of $578,000 for 37 noncompeting fellowships represents the continuation cost of fellowship awards made in 1974.

   b. The amount of $482,000 in competing fellowships represents 33 new awards.

3. Training grants:

   a. The increase of $108,000 in noncompeting training grants represents the continuation cost for 2 awards made in 1974.

4. Research and development contracts--The increase of $330,000 would provide for 4 additional research contracts.

5. Intramural laboratory and clinical research--The increase of $868,000 would permit the expansion of our intramural research program in the areas of environmental mutagenesis and reproductive toxicology and etiology of environmental diseases and disorders.

Decreases:

A. Built-in--The decrease of $85,000 reflects the annualization of savings resulting from prior year employment reductions.

B. Program:

1. Research grants:
    a. The decrease of $2,798,000 represents 45 noncompeting regular research grants that were completed in 1974 or that will be converted to competing status in 1975.
    b. The decrease of $6,624,000 reflects the conversion of 98 competing grants to a noncompeting status.
    c. The decrease of $1,365,000 reflects the reduced funding required in 1975 due to the multi-year funding of 24 competing projects in 1974.
2. Fellowships:
    a. The decrease of $16,000 represents 1 noncompeting fellowship that was completed in 1974.
    b. The decrease of $575,000 reflects the conversion of 37 competing fellowships to a noncompeting status, and the completion of 2 awards.
3. Training grants:
    a. The decrease of $1,603,000 represents 5 noncompeting training grants terminated in 1974, and a reduction in the funding level for the balance of the program.
    b. The decrease of $1,202,000 represents the conversion of $108,000 and 2 training grants to noncompeting status and $1,094,000 for administrative supplements.

Obligations by Activity

Page Ref.		1974* Base		1975 Estimate		Increase or Decrease		
		Pos.	Amount	Pos.	Amount	Pos.	Amount	
145	Environmental health sciences centers...	---	$4,000,000	---	$5,100,000	---	+$1,100,000	A
147	Environmental mutagenesis and reproductive toxicology	---	2,150,000 (2,983,000)	---	2,800,000	---	+650,000	B
149	Etiology of environmental diseases and disorders..........	---	4,385,000 (5,539,000)	---	4,100,000	---	-285,000	C
153	Environmental pharmacology and toxicology.........	---	5,881,000 (7,709,000)	---	4,334,000	---	-1,547,000	D
155	Environmental pathogenesis......	---	2,340,000 (2,889,000)	---	1,810,000	---	-530,000	E
157	Intramural laboratory and clinical research..........	197	8,203,000	197	9,158,000	0	+955,000	F
159	Research management and program services.........	38	1,379,000	38	1,382,000	0	+3,000	G
	Total obligations (base).	235	28,338,000	235	28,684,000	0	+346,000	
	Total obligations........		(32,702,000)					

*Base - Excludes 1973 appropriation restorations. Total obligations shown in parenthesis.

Explanation of Changes (by activity)

A) Environmental health sciences centers--The increase of $1,100,000 would permit the Institute to initiate 1 new center, and provide for the increased continuation costs of the currently active programs.

B) Environmental mutagenesis and reproductive toxicology--The increase of $650,000 would permit the funding of 20 additional research grants and fellowships, and 1 additional research contract, offset by a decrease of 1 training award. The funds requested will facilitate the development and evaluation of new mutagenesis testing methods with direct quantitative relevance to man.

C) Etiology of environmental diseases and disorders--Because of a projected decrease in the average cost of supported research grants, training grants, and contracts, the $285,000 reduction in funds requested would result in a net increase of 17 supported projects. The increase in supported projects will be 9 research grants, 7 fellowship awards, and 1 additional training award. The funds requested will permit a somewhat broader effort in exploring the biological effects of new chemical agents and potentially harmful physical factors.

D) Environmental pharmacology and toxicology--The decrease of $1,547,000 results in a net increase of 5 supported projects, primarily because of the projected 70% increase in numbers of fellowships. Fellowships and research contracts will increase by 14, offset by a decrease of 9 research grant and training awards. The funds requested would permit the continuation of research directed at the clarification of the mechanisms by which environmental agents act.

E) Environmental pathogenesis--The decrease of $530,000 results in a net increase of 4 supported projects, primarily because of a projected decrease in the average cost of supported grants and contracts. Fellowships and research contracts will increase by 8, offset by a decrease of 4 research grants. The funds requested will permit the continuation of research directed at defining the pathological events in disease development.

F) Intramural laboratory and clinical research--The total increase of $955,000 contains $87,000 for built-in requirements and $868,000 for a program increase. This increase will permit the expansion of our intramural research program in the areas of environmental mutagenesis and reproductive toxicology and etiology of environmental diseases and disorders.

G) Research management and program services--The total increase of $3,000 is for mandatory costs.

Obligations by Object

	1974 Estimate	1975 Estimate	Increase or Decrease
Total number of permanent positions......................	235	235	0
Full-time equivalent of all other positions................	90	95	+5
Average number of all employees..	331	328	-3
Personnel compensation:			
Permanent positions............	$3,567,000	$3,582,000	+$15,000
Positions other than permanent.	587,000	625,000	+38,000
Other personnel compensation...	110,000	120,000	+10,000
Subtotal, personnel compensation...............	4,264,000	4,327,000	+63,000
Personnel benefits...............	436,000	442,000	+6,000
Travel and transportation of persons.........................	320,000	350,000	+30,000
Transportation of things.........	27,000	30,000	+3,000
Rent, communications and utilities.........................	980,000	990,000	+10,000
Printing and reproduction........	50,000	60,000	+10,000
Other services...................	1,388,000	1,496,000	+108,000
Project contracts.............	2,000,000	2,330,000	+330,000
Payment to NIH Management Fund.	792,000	855,000	+63,000
Supplies and materials...........	825,000	1,390,000	+565,000
Equipment........................	500,000	600,000	+100,000
Grants, subsides and contributions.................	21,120,000	15,814,000	-5,306,000
Total obligations by object..	32,702,000	28,684,000	-4,018,000
Total obligations excluding 1973 appropriation..............	28,338,000		

Significant Items in House and Senate Appropriations Committee Reports

Item

1974 Senate Report	Action taken or to be taken
New Methods of Safety Testing	
1. "The committee will expect that a portion of the congressional increase is used to accelerate the Institute's efforts to establish better methods of safety testing and to strengthen the development of the mutagenesis programs so that more can be learned about the extent to which environmental agents threaten the development of future generations." (Page 58)	1. The 1974 Congressional increases were to restore the Institute's programs to the 1972 level. Within those amounts, the Institute has significantly increased its research program in mutagenesis. It has continued to emphasize fundamental studies which will provide the scientific base for future applied efforts in safety testing.

Authorizing Legislation

Legislation	1975	
	Authorization	Appropriation Requested
Public Health Service Act		
Section 301--Research and Investigation, in general........................	Indefinite	$28,684,000
Title III, Part A--National Institute of Environmental Health Sciences...	Indefinite	

National Institute of Environmental Health Sciences

Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
1965	$10,920,000	$ 9,380,000	$ 9,730,000	$ 9,380,000
1966	15,933,000	15,933,000	15,983,000	15,983,000
1967	24,312,000	24,298,000	24,298,000	24,298,000
1968	19,896,000	16,570,000	19,896,000	16,570,000
1969	17,548,000	16,990,000	17,548,000	17,269,000
1970	17,777,000	17,777,000	17,777,000	17,777,000
1971	19,397,000	20,067,000	21,067,000	20,067,000
1972	24,840,000	25,945,000	31,445,000	25,945,000
1973*	28,532,000	30,412,000	30,412,000	30,412,000*
1974	25,263,000	28,879,000	28,879,000	28,820,000**
1975	28,684,000			

* Note: This appropriation authority was the continuing resolution. The appropriation amount was the House Allowance, which was the lower of the House or Senate amounts in the first vetoed bill.

** Appropriation after reduction - $28,338,000

Justification

National Institute of Environmental Health Sciences

	1974* Base		1975		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits..	235	$4,700,000	235	$4,769,000	0	+$69,000
Other expenses..	---	23,638,000	---	23,915,000	---	+277,000
Total.........	235	28,338,000	235	28,684,000	0	+346,000

General Statement

The National Institute of Environmental Health Sciences seeks to increase our understanding of the extent to which environmental agents can adversely affect man's health either immediately or over time. The results of the Institute's research are promptly made available to agencies having responsibility for environmental monitoring, standard setting, and control. The Institute seeks to determine the magnitude and significance of the hazard to man's health resulting from exposures to a wide range of concentrations of chemical, physical, and biological agents in the environment. Underlying mechanisms of adverse response are examined in order to determine the principles and generalizations which can provide the criteria needed to serve as a basis for the establishment of standards by those agencies charged with the regulatory responsibility in this area.

Among the beneficiaries of the basic knowledge developed by the Institute are those professionals concerned with the environmental components of human disease - e.g. - physicians treating poisonings by environmental chemicals; and medical teams concerned with the etiology of new diseases peculiar to certain locales or puzzled by drug interactions with environmental components. Our data are also useful to other programs dealing with environmental components of cancer, mutagenesis or heart and lung diseases (e.g. - National Cancer Institute, National Institute of Child Health and Human Development; National Heart and Lung Institute). Close liaison is maintained between the Institute and the academic and medical communities as well. Liaison is also maintained between NIEHS and other Governmental agencies concerned with the environment -- Environmental Protection Agency, Food and Drug Administration, and National Institute of Occupational Safety and Health. Such contacts maintain awareness of programs, avoid unnecessary duplication of efforts, and foster supportive collaboration.

Extramural Research

Grant support of research in the environmental health sciences is an essential component of the national effort to identify, characterize, and ultimately deal with or regulate hazards in the environment. Fundamental data coming from research on environmental toxicants and their mechanisms of action suggest new solutions to the complex and growing problems of environmental contamination. As the information base expands and new techniques of measurement and analysis are developed, new approaches to realistic control methods or standards can be developed.

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* Excludes 1973 appropriation restorations.

Intramural Research

The Institute's intramural program at NIEHS investigates the actions, interactions, and mechanisms of actions of environmental components on biological systems including, where possible, the comparison of these effects with those in man. Such information is sought in order to provide a basis for the prevention, early diagnosis, and treatment of environmentally-related or affected diseases in man, and to establish the scientific basis for removal of agents from the environment.

The Institute's extramural and intramural programs are a blend of fundamental and applied research efforts applied to areas in which the state of knowledge justifies broad scale investigation. They, therefore, serve as a prime and unique focus for National and International efforts to deal with the effects of the environment on man's health.

The narrative material which follows provides information about current and planned investigation, for support or conduct of research through grants, contracts, and in the Institute's own laboratories. The Institute's activities are discussed here in terms of programs. They are planned and operated as part of a total national program with each component complementary to the others, and all directed toward understanding of hazards to health resulting from man's interaction with his environment.

DHEW - National Institutes of Health

CROSSWALK - 1974 COLUMN 1975 PRESIDENT'S BUDGET

INSTITUTE: National Institute of Environmental Health Sciences
(In thousands)

Mechanism / Program	Research Grants										
	Regular Program			Specials		Training Programs		Laboratory and Clinical Research	Research and Development Contracts	Other Direct Operations	TOTAL
	Non-competing	Competing	Subtotal	Multi-disciplinary Centers	Other	Grants	Fellowships				
1974 Base Obligations											
1. Environmental health sciences centers	---	---	---	$4,000	---	---	---	---	---	---	$4,000
2. Environmental mutagenesis and reproductive toxicology	$322	$759	$1,081	---	$5	$66	$137	---	$861	---	2,150
3. Etiology of environmental diseases and disorders	2,284	1,036	3,320	---	57	527	106	---	375	---	4,385
4. Environmental pharmacology and toxicology	2,680	1,246	3,926	---	101	1,383	242	---	229	---	5,881
5. Environmental pathogenesis	984	476	1,460	---	20	219	106	---	535	---	2,340
6. Intramural laboratory and clinical research	---	---	---	---	---	---	---	$8,203	---	---	8,203
7. Research management and program services	---	---	---	---	---	---	---	---	---	$1,379	1,379
Subtotal	6,270	3,517	9,787	4,000	183	2,195	591	8,203	2,000	1,379	28,338
Unobligated Balance Restored											
1. Environmental mutagenesis and reproductive toxicology	---	777	777	---	20	36	---	---	---	---	833
2. Etiology of environmental diseases and disorders	---	866	866	---	---	288	---	---	---	---	1,154
3. Environmental pharmacology and toxicology	---	1,056	1,056	---	---	757	15	---	---	---	1,828
4. Environmental pathogenesis	---	408	408	---	20	121	---	---	---	---	549
Subtotal	---	3,107	3,107	---	40	1,202	15	---	---	---	4,364
Total obligations	6,270	6,624	12,894	4,000	223	3,397	606	8,203	2,000	1,379	32,702

DHEW - National Institutes of Health

CROSSWALK - 1975 COLUMN 1975 PRESIDENT'S BUDGET

INSTITUTE: National Institute of Environmental Health Sciences
(In thousands)

Mechanism	Research Grants										
	Regular Program			Specials		Training Programs		Laboratory and Clinical Research	Research and Development Contracts	Other Direct Operations	TOTAL
Program	Non-competing	Competing	Subtotal	Multi-disciplinary Centers	Other	Grants	Fellowships				
1. Environmental health sciences centers........	---	---	---	$5,100	---	---	---	---	---	---	$5,100
2. Environmental mutagenesis and reproductive toxicology.............	$1,131	$359	$1,490	---	$40	---	$220	---	$1,050	---	2,800
3. Etiology of environmental diseases and disorders..	2,512	753	3,265	---	45	$228	212	---	350	---	4,100
4. Environmental pharmacology and toxicology..........	2,609	444	3,053	---	118	382	431	---	350	---	4,334
5. Environmental pathogenesis	789	119	908	---	20	90	212	---	580	---	1,810
6. Intramural laboratory and clinical research.......	---	---	---	---	---	---	---	$9,158	---	---	9,158
7. Research management and program services........	---	---	---	---	---	---	---	---	---	$1,382	1,382
Total obligations.........	7,041	1,675	8,716	5,100	223	700	1,075	9,158	2,330	1,382	28,684

National Institute of Environmental Health Sciences
Budget Mechanism

	1974*		1975	
	Number	Amount	Number	Amount
Grants				
Regular				
Non-competing	91	$6,270,000	120	$7,041,000
Competing	18	1,591,000	9	608,000
New	31	1,861,000	22	992,000
Supplemental	(4)	65,000	(5)	75,000
Subtotal	140	9,787,000	151	8,716.000
Special				
Environmental health sciences centers	6	4,000,000	7	5,100,000
Research career programs	7	159,000	9	195,000
Scientific evaluation	---	24,000	---	28,000
Subtotal	13	4,183,000	16	5,323,000
Total Grants	153	13,970,000	167	14,039,000
Fellowships				
Non-competing	3	31,000	39	593,000
Competing	---	---	---	---
New	37	560,000	33	482,000
Supplemental	---	---	---	---
Subtotal	40	591,000	72	1,075,000
Training Grants				
Non-competing	21	2,195,000	18	700,000
Competing	---	---	---	---
New	---	---	---	---
Supplemental	---	---	---	---
Subtotal	21	2,195,000	18	700,000
Laboratory and clinical research		8,203,000		9,158,000
Research and development contracts		2,000,000		2,330,000
Research management and program services		1,379,000		1,382,000
TOTAL		28,338,000		28,684,000

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* Excludes 1973 appropriation restorations.

Environmental Health Sciences Centers

Authorizing Legislation: Public Health Service Act, Title III, Part A

	1974* Base		1975		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits..	---	---	---	---	---	---
Other expenses..	---	$4,000,000	---	$5,100,000	---	+$1,100,000
Total.........	---	$4,000,000	---	$5,100,000	---	+1,100,000

Introduction

The University-based Centers serve to integrate the efforts of scientists in several traditional disciplines and foster application of expertise across disciplinary lines to environmental health problems. The Centers are characteristically made up of groups of scientists who collaborate to develop fundamental and practical information about the causes and nature of environmental diseases in order to guide corrective and therapeutic programs. Because of the variety and complexity of environmental problems, several Centers with complementary spheres of interest are required to fulfill the national need. Accordingly, six Centers, each with special expertise in one or more of the major categorical programs of the Institute, are supported. Collectively, they provide outstanding capabilities in traditional basic and applied disciplines vital to the Institute program including, among others, chemistry, cell biology, genetics, physiology, biostatistics, pharmacology, toxicology, pathology, epidemiology, behavioral sciences, nutritional science, occupational medicine, and chemical and environmental engineering.

Program Plans for 1974 and 1975

Each of the Centers, in accord with the specialties and research expertise of its staff, makes important contributions to the programs of the Institute. Their studies deal both with hazardous agents in the environment, which are the immediate focal points of public concern, and with specific diseases and disorders of environmental origin, which constitute the long-term basis for concern. Advances are being made in the identification and characterization of the sources, modes of entry, sites and basis of cell and tissue damage, and persistence of known and potential noxious agents. Important new data and insights are being developed regarding specific environmentally-related health problems, including chemical carcinogenesis; teratogenesis, and other reproductive disorders; neural and behavioral anomalies; respiratory, circulatory, and kidney diseases; and fundamental aspects of toxicant metabolism and disruptive interactions at the molecular and cellular levels. Further advances are also being made in long-term population studies with emphasis on chemical epidemiology and on methodology for detecting early symptoms of fibrotic diseases of the lung, emphysema, and other disorders associated with occupational or accidental exposure to environmental chemicals and dusts.

The University-based Centers are national resources with concentrated expertise in areas of primary responsibility of the Institute. The new Center established in 1973 fills an important gap in epidemiology of lung and other diseases associated with industrial and urban environments. A new Center, which will focus on all aspects of heavy metals as etiological agents and on pathogenesis, is being planned for activation within the next year. The ongoing Centers will continue their work in a wide range of environmental health problems.

*Excludes 1973 appropriation restorations.

The increase of $1,100,000 would permit the Institute to initiate 1 new University-based Center and provide for the increased continuation costs of the currently active program.

Environmental Mutagenesis and Reproductive Toxicology

Authorizing Legislation: Public Health Service Act, Title III, Part A

	1974[*] Base		1975		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits..	---	---	---	---	---	---
Other expenses..	---	$2,150,000	---	$2,800,000	---	+$650,000
Total.........	---	2,150,000	---	2,800,000	---	+650,000

Budget Mechanism:	No.	Amount	No.	Amount	No.	Amount
Research Grants:						
Regular....	18	1,081,000	30	1,490,000	+12	+409,000
Special....	—	5,000	2	40,000	+2	+35,000
Subtotal.	18	1,086,000	32	1,530,000	+14	+444,000
Fellowships	9	137,000	15	220,000	+6	+83,000
Training grants....	1	66,000	---	0	-1	-66,000
Research & development contracts.	9	861,000	10	1,050,000	+1	+189,000
Total....	37	2,150,000	57	2,800,000	+20	+650,000

Introduction

The mutagenesis and reproductive toxicology program deals with environmental phases of reproduction and fetal development. Clarification of interaction between chemical agents found in air, water, food and occupational situations and changes in the genetic makeup of man, his reproductive capability, and in the development of the embryo or fetus. Induction of permanent changes in human genetic material is without question the most profound danger associated with environmental agents. In addition to anatomical defects generally ascribed to mutations, it is clear that subtle deficits in mental capacity and susceptibility to degenerative and infectious diseases also result from genetic aberrations. A major obstacle in assessing mutagenic potential of chemical agents has been the lack of rapid, inexpensive test systems with unequivocal quantitative relevance to man. This program is designed to fill this gap and supports substantial effort, aimed at the development of sensitive test systems for detection and quantification of mutations.

Plans for 1974 and 1975

Advances are being made toward further understanding of the chemistry of molecular interactions between DNA and mutagenic agents such as azides, polychlorinated biophenyls (PCBs), and nitroso compounds. Such studies should provide an understanding of the molecular basis of visible changes in biochemistry and morphology and serve as a guide in devising test procedures to determine the frequency of mutations caused by different classes of mutagens. Efforts are being made to assess existing mutagenesis test procedures for relevance to man and toward development of new procedures. This is a high priority aspect of the program. The Institute recognizes serious deficiencies in available mutagenesis testing procedures, and in almost all cases the relevance of existing methodology to man at realistic mutagen levels is questionable. It recognizes also the necessity to establish valid tests as a basis for further and more rapid progress in this area. In line with this, new initiatives are needed to interest the scientific community in applying the necessary effort and expertise for development of human mutagenicity test systems.

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[*] Excludes 1973 appropriation restorations.

In reproductive toxicology the agents of primary concern are widespread compounds such as organophosphate and chlorinated hydrocarbon insecticides, PCBs, dioxins, mercurials and toxic fungal metabolites sometimes associated with foodstuff. The studies range from efforts to establish causal relationships between toxicants and specific disorders to those designed to elucidate the molecular and cellular basis of hormonal changes and teratogenesis.

In the case of PCBs, multigeneration effects on reproduction were studied. It was found that though the compounds appear to have no effects at very low levels on genes or reproduction during the first generation, continued exposure over several generations results in chromosomal damage and birth defects. This study points up the necessity for long-term and multigeneration testing in assessing the potential hazard of persistent toxicants to man.

Several studies focus on the relationship between gestational periods and the nature and degree of damage induced in the fetus by certain pesticides and fungal toxins. These studies shed further light upon both the maximum risk time during gestation and the relationship between time of exposure and the nature of deformities in the offspring.

The importance of this program in maintaining the genetic fidelity of mankind and in assuring the conception and delivery of healthy babies now and in the future cannot be overemphasized. Thus, ongoing programs will be continued and during the coming year efforts will be made to apply the skills of geneticists and scientists in related fields to bear upon pressing problems in this area.

Etiology of Environmental Diseases and Disorders

Authorizing Legislation: Public Health Service Act, Title III, Part A

	1974[*] Base		1975		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits..	---	---	---	---	---	---
Other expenses..	---	$4,385,000	---	$4,100,000	---	-$285,000
Total.........	---	4,385,000	---	4,100,000	---	-285,000

Budget Mechanism:	No.	Amount	No.	Amount	No.	Amount
Research grants:						
Regular......	43	3,320,000	52	3,265,000	+9	-55,000
Special......	2	57,000	2	45,000	0	-12,000
Subtotal...	45	3,377,000	54	3,310,000	+9	-67,000
Fellowships..	7	106,000	14	212,000	+7	+106,000
Training grants......	6	527,000	7	228,000	+1	-299,000
Research and development contracts...	4	375,000	4	350,000	0	-25,000
Total	62	4,385,000	79	4,100,000	+17	-285,000

Introduction

The central objective of the etiology program is to establish causal associations between human diseases and environmental chemicals and physical factors. It includes broad surveys aimed at identifying chemical agents now in use, or proposed for use, that have adverse effects upon biological systems. Concomitantly, it deals with description of specific malfunctions produced by these agents in body organs. This research provides a sound basis for clinical recognition of environmentally-related disorders in man, determination of their causes, and implementation of correct therapeutic and preventive measures. In a broader sense, it generates understanding of quantitative relationships between human diseases and noxious environmental agents. This understanding will serve as a basis for rational management of current technology and future industrial development in such a way as to make them compatible with human health and well-being.

Program Plans for 1974 and 1975

Thousands of new chemicals are synthesized each year. Many of these are brought into large scale production, adding to several hundred thousand already in use in industry to make home and personal care products, pesticides, pharmaceuticals, fuel and food additives and a host of others. Despite increased efforts by manufacturers and government agencies to test new and existing compounds, the biological effects of many chemicals, physical factors, and combinations of these are unknown. Grantees are continuing to provide new insight into dose-disease relations for a broad range of agents.

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[*] Excludes 1973 appropriation restorations.

By use of newly developed techniques and models, some pesticides have been found to disrupt nerve function and to influence behavioral and learning patterns. Though similar effects have not yet been demonstrated in man, the studies indicate the potential of these compounds to modify man's behavior. Further probing of the long-term effects of mercury and lead in the central nervous system have also revealed adverse effects on learning and behavior. The effects are seen in experimental animals which exhibit no visible lesions in the nervous system. Studies of this nature add a new dimension to problems of detection of cause-effect relations. They indicate the need to reassess our thinking in regard to meaningful dose-endpoint relations, and in regard to appropriate environmental tolerance levels.

Research on the isolation and toxicity of natural and synthetic substances in food is being supported. Four toxins induced in sweet potato by injury or disease were isolated and identified. These toxins cause massive accumulation of fluids in the lungs of experimental animals, and three of the four cause kidney damage. Carcinogenic compounds and substances which cause kidney damage and blindness were found in fungi that infest food grains. Aflatoxin, an extraordinarily potent carcinogenic by-product from certain fungi, was shown for the first time to cause cancer in fish through exposure of the eggs to the compound. Nitrites used as food additives were shown to react with sarcosine and other amines to form nitroso derivatives, a class of compounds known to be potent carcinogens and at least mild mutagens. This indicates the possibility of formation of carcinogens in the stomach and raises again the potential hazard of nitrites in foods.

The influence of heat, light, noise, microwaves, and laser radiation on human well-being is being investigated. Light was shown to enhance the acute toxicity of certain hepatotoxins such as aflatoxin, apparently through activation mechanisms in which riboflavin plays a role. Laser radiation was shown also to activate certain natural pigments. Activated forms of these pigments appear to be responsible for tissue lesions associated with laser radiation.

Work on air pollutants as etiological agents continues to produce new insight into diseases and disorders of the lungs and cardiovascular system. Ozone and nitrogen dioxide affect the lung lining through destruction of fatty substances. Sulfur dioxide from the air and sulfites used as food preservatives interact with some sulfur-containing compounds, forming thiosulfonates. These compounds circulate in the blood stream, slowly releasing sulfite throughout the body. Hydrazine, used in making a number of useful products, produces lesions characteristic of diabetes in experimental animals. Dichloroethylene and other compounds used in the plastics industry were found to be liver toxins and carcinogens which present considerable hazards to workers.

Further epidemiological studies on asbestosis revealed heretofore unrecognized dangers associated with asbestos inhalation. Cancer of the lungs and a rare cancer of the lung and abdominal linings, called mesothelioma, occur more frequently in insulation workers and others in building trades who are exposed to relatively small amounts of asbestos. Moreover, the probability of cancer may be increased up to 50-fold in these workers if they are also heavy smokers. These findings led to initiation of quantitative time-dose studies on the general population in urban areas, because residents of large cities are subjected to substantial levels of asbestos and other potentially carcinogenic air pollutants throughout their lives.

Further studies were carried out on the health effects of carbon monoxide. In addition to the limitations this gas imposes on the oxygen carrying capacity of the blood, high levels of carbon monoxide also alter blood flow to the abdominal region and may contribute to fatty accumulations in the blood and in arterial and heart muscles, thus aggravating preexisting cardiovascular disorders.

The importance of the agents and the scope of disorders indicated emphasize the necessity for continued effort to establish associations between these agents and disease and physiological stresses. Despite the difficulties of testing all environmental agents and combinations of agents, some new principles are beginning to emerge which permit cautious generalizations with respect to etiological relations of classes of compounds. This will materially reduce the burden of massive testing of individual compounds. New projects will be undertaken to further the progress toward establishing such principles and generalizations. Work will also continue on the hazards of specific agents in carcinogenesis, teratogenesis, lung and cardiovascular diseases, neurotoxicity and other less debilitating but costly disorders and degeneratives processes.

Environmental Pharmacology and Toxicology

Authorizing Legislation: Public Health Service Act, Title III, Part A

	1974 * Base		1975		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits.......	---	---	---	---	---	---
Other expenses.......	---	$5,881,000	---	$4,334,000	---	-$1,547,000
Total..............	---	5,881,000	---	4,334,000	---	-1,547,000

Budget Mechanism:	No.	Amount	No.	Amount	No.	Amount
Research Grants:						
Regular..........	57	3,926,000	51	3,053,000	-6	-873,000
Special..........	4	101,000	4	118,000	0	+17,000
Subtotal.......	61	4,027,000	55	3,171,000	-6	-856,000
Fellowships........	17	242,000	29	431,000	+12	+189,000
Training grants....	12	1,383,000	9	382,000	-3	-1,001,000
Research and development contracts...	2	229,000	4	350,000	+2	+121,000
Total......	92	5,881,000	97	4,334,000	+5	-1,547,000

Introduction

The pharmacology-toxicology program is designed to develop understanding of the principles and mechanisms involved in toxicity of environmental agents. The research ranges from mechanistic studies of factors that alter the toxicity of chemical agents to studies on absorption and transport within the body. The nature and sites of defense systems and molecular targets associated with visible functional disorders are also being investigated. The goal is to provide a rational basis for maintaining, through environmental management, reasonable safety margins between environmental and body burdens of toxic agents in order to safeguard human health now and in future generations.

Program Plans for 1974 and 1975

Past work has shown that many organic compounds are susceptible to transformation by light, UV (ultraviolet) and other factors in the environment and by the action of various enzymes in the body. While nontoxic substances are generally formed, more toxic compounds are sometimes generated. Continuing studies show that aromatic petroleum products, common as air pollutants in urban areas, give rise to carcinogenic agents. Several pesticides, particularly, aldrin and dieldrin, are converted to more toxic derivatives upon exposure to sunlight. These studies provide a clearer understanding of hazardous compounds in the environment and facilitate attempts to clarify toxicity mechanisms.

The mode of action of several metals was investigated. Zinc was found to protect the lungs against damage by low levels of ozone and nitrous oxide. Cadmium and lead have a similar but less marked effect.

Further advances were made toward understanding the clinical, pharmacological and biochemical aspects of lead and mercury intoxication. Lead impairs the operation of mixed function oxidases and, as a result, causes lead intoxicated

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*Excludes 1973 appropriation restorations.

children to exhibit reduced metabolism of drugs and male hormones. In some cases, this may present a health hazard.

New chelating agents effective in antagonizing the toxicity of methylmercury salts are being developed. Natural defense systems against heavy metals have also been demonstrated. At least four proteins have been identified which form strong complexes with cadmium, lead and mercury. These appear to play a part in combating heavy metal toxicity and may provide a useful means of protection against the hazards of heavy metal exposure.

Studies are continuing on the nature of drug metabolizing enzymes. These enzymes generally detoxify foreign agents and make them more readily excreted through the kidneys, However, in some cases, the same enzymes activate carcinogenic agents, such as benzpyrene and aflatoxin, and facilitate the development of cancer. Attempts are being made to gain further insight into the mechanisms that regulate these activities.

Parallel advances are being made in analytical methodology which forms the foundation for progress in quantitative toxicology and pharmacology. A new instrument was developed which will detect 0.5 parts per trillion of the potent teratogen dioxin in cells and tissues. This provides analytical capability for further advancement of understanding of quantitative aspects of dioxin toxicity and teratogenicity. The instrument and principles on which the procedure is based can be applied also to analysis of other chlorinated compounds for which methodology was previously inadequate. Advances are being made in techniques for monitoring body burdens and exposures to nitrous oxide, sulfur dioxide and carbon monoxide.

Understanding of the movement and sites of action of toxic agents is vital in establishing the risk-benefit equation in modern technology. New projects will continue to focus on transformations of compounds in order to understand the nature of proximal toxicants and their subsequent effects on cellular and tissue targets. In many cases, interactions between combinations of compounds result in dangerous enhancement of toxicity even at levels at which the individual agents are normally considered to present no risk to man. Such interactions must be identified and assessed for their consequences in relation to long-term health problems and the risk of birth defects and genetic change in future generations.

Environmental Pathogenesis

Authorizing Legislation: Public Health Service Act, Title III, Part A

	1974* Base		1975		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits..	---	---	---	---	---	---
Other expenses..	---	$2,340,000	---	$1,810,000	---	-$530,000
Total.........	---	2,340,000	---	1,810,000	---	-530,000

Budget Mechanism:	No.	Amount	No.	Amount	No.	Amount
Research Grants:						
Regular.....	22	1,460,000	18	908,000	-4	-552,000
Special.....	1	20,000	1	20,000	0	0
Subtotal..	23	1,480,000	19	928,000	-4	-552,000
Fellowships.	7	106,000	14	212,000	+7	+106,000
Training grants.....	2	219,000	2	90,000	0	-129,000
Research and development contracts..	5	535,000	6	580,000	+1	+45,000
Total...	37	2,340,000	41	1,810,000	+4	-530,000

Introduction

The pathogenesis program focuses upon the details and time sequence of molecular and cellular events that culminate in recognizable diseases and endpoints upon exposure of individuals to toxic agents. Because of the wide range of chemical agents and physical factors present, no organ or body function can be considered invulnerable. Diseases of the pulmonary and cardiovascular systems, the liver, kidneys, reproductive system, digestive tract, the central and peripheral nervous systems, and degenerative disorders of complex and long-term etiology have been documented and related to one or more environmental agents. Additionally, the program is intended to clarify the interactions through which environmental agents play a secondary or ancillary role in the progress of degenerative disorders. Knowledge of initial or very early molecular and cellular lesions and understanding of their role in pathological endpoints offers the best hope, apart from prevention of toxic exposures, for detecting and countering the development of diseases before damage in target organs become irreversible and progressive.

Plans for 1974 and 1975

Studies on the biologic effects of radiation have led to development of lighting systems that closely simulate natural noon sunlight. This has permitted critical experiments in phototoxicity and light-induced cancer. As a result, new insights into the induction and potentiation of such cancer by chemical agents are being developed. Similar studies are underway to assess the role of light intensity and quality in photosensitization phenomena in certain other skin diseases and allergies.

* Excludes 1973 appropriation restorations.

Studies are underway currently to assess the long-term effects and mechanisms of heat stress, dehydration, microwaves and other physical factors in aging and degenerative diseases associated with aging.

Studies were carried out on the process of transition from normal to cancerous cells and the possible role of various environmental factors in the transition. The findings indicate that cancer formation may involve several rather distinct steps: the first step is called initiation, which may result from a somatic mutation; the second a promotion phase, in which normal suppression of cell division no longer prevails; and the third is a phase of rapid cell growth. The second, or promotion stage, can be inhibited by proteases, which suggests that a protein is involved in tumorigenesis and that ways might be found to block cancer formation at this stage.

Studies have been conducted on pathogenesis induced by heavy metals. They show that lead accumulates at the endplate region of the juncture between nerve and muscle fibers, blocking electrical impulses and preventing transmission of messages from the brain to the muscle. Both lead and mercury damage the sheath in nerve fibers and destroy the selectivity in passage of substances from the blood into the brain, thereby disrupting the chemical balance in the central nervous system. These studies help to clarify the basis of the behavioral and learning aberrations characteristic of lead and mercury poisoning of long duration.

Similar studies on renal disorders induced by these metals and their compounds show disruption of selective absorption processes and interference in energy metabolism and protein synthesis. This may account for malfunction in the absorptive mechanism.

Important contributions were being made toward understanding fibrotic diseases of the lungs, including asbestosis and berylliosis. Triggering of connective tissue biosynthesis appears to be the first step in these diseases. It was shown that beryllium forms an antigenic complex with normal lung protein, which gives rise to fibrotic lesions. Other basic studies reveal that certain dusts and chemicals of environmental origin destroy the normal antiproteinase factors in the lungs, permitting over-activity of protein digesting enzymes. This presumably leads eventually to digestion of vital lung tissues and results in emphysema.

Many other fundamental studies are currently underway to determine effects of environmental chemicals and dusts on cilia and lung macrophages in the respiratory tract and the consequences of inactivation of these cells in terms of development of chronic bronchitis, emphysema, fibrosis and other lung disorders.

Although considerable progress has been made, much remains to be done to develop a clear understanding of all ramifications of environmental agents in acute and chronic disease development and new and ongoing projects will continue to focus on these problems.

Intramural Laboratory and Clinical Research

Authorizing Legislation: Public Health Service Act, Title III, Part A

	1974* Base		1975		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits........	197	$3,944,000	197	$3,998,000	0	+$54,000
Other expenses........	---	4,259,000	---	5,160,000	---	+901,000
Total..............	197	8,203,000	197	9,158,000	0	+955,000

Introduction

The intramural research program is directed toward development of a reliable data base for use in establishing standards and devising remedial methods in a variety of populations at risk from exposure to environmental and occupational chemicals and physical factors. The Institute is fostering research at the fundamental level on a wide range of environmental agents and on the mechanisms of acute and long-term effects of these agents on man. The program is focused on several environmental problems which, on the whole, present the greatest potential hazard to the present population and future generations. These include airborne toxicants, metal toxicants, pesticides, mutagenic compounds, physical factors, and noncategorical hazardous compounds.

Plans for 1974 and 1975

The studies on airborne toxicants focus on compounds which generally gain entry into the body through the lungs, although entry through the skin and gastrointestinal tract may also occur as a result of settling on the skin and into food and water supplies. Numerous human diseases and disorders from exposure to such agents are now well established. These include berylliosis, asbestosis, emphysema, chronic bronchitis, lung cancer, cardiovascular diseases, and reproductive disorders and fetal anomalies. A considerable portion of intramural facilities are devoted to special monitoring and metering devices for conducting long-term studies on the interrelationships between airborne agents and various disorders in experimental mammalian models.

Several scientists have devoted their full efforts to developing basic information about the sites and mode of action of heavy metals. Special attention has been given to mercury and lead and their compounds. Understanding of the biochemical and structural basis of neurological and teratogenic effects of these substances has been notably advanced.

Intensive effort has been devoted to clarification of the many aspects of pesticide interactions in mammalian systems. Pesticides are an extremely diverse group of compounds with widely differing chemical structures and properties. Not surprisingly, therefore, they exhibit a broad spectrum of biological activities ranging from general toxicity to specific targeted action on nerve tissues and often on specific enzymes and processes. Institute scientists have concerned themselves with all aspects of pesticide toxicology, including structure-activity relationships, metabolism, pharmacodynamics, mechanisms of actions, and mechanisms of detoxication and toxicity enhancement. Considerable effort has been devoted also to clarification of joint action of the various compounds on concomitant multiple exposure in disorders such as birth defects, carcinogenesis, mutagenesis, and general toxicity.

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*Excludes 1973 appropriation restorations.

As part of the Institute's overall efforts in the area of mutagenesis, the intramural efforts have been greatly intensified. Work is continuing at an accelerated pace on the nature of mutagens and their interactions with DNA. Efforts are continuing also on refinement of the host mediated assay for assessment of mutagenic potential and mechanisms of suspected and known mutagens. However, special emphasis is placed upon development of in vivo test procedures which will detect point mutations and can be used to bridge the gap between test models and mutation frequency and susceptibility in man. This is a high priority goal of the Institute and maximum effort will continue in this area. This work is designed to protect the genetic integrity of the present population and future generations.

Progress has been made toward establishing quantitative relationships between biological effects of physical factors in the field of noise, microwaves, and radiation. Because of the paucity of research in these areas and the importance of these factors in human well-being, work in the intramural program is being expanded.

In addition to the work in the categories mentioned, a considerable effort is devoted to problems which are not included in these programs. The agents involved are diverse and include toxic metabolites of fungi, products from higher plants and animals, and numerous medicants and industrial compounds. Some of these are implicated as causative in cancer, birth defects, reproductive anomalies, and numerous less well-defined disorders. Studies on these substances and the disorders they cause are more restricted in scope than in the categorical programs. However, the same general aims of developing a data base for appropriate control of the compounds and amelioration of their effects prevail in all studies.

The intramural program provides the vehicle for direct research to deal with problem areas and specific problems vital to the national interests and to the fulfillment of Institute responsibilities where sufficient effort and interest is not available elsewhere in the scientific community. In many instances, projects and research developments within the intramural program serve as a catalyst to the scientific community at large. Work will continue in the areas indicated and new projects, especially in mutagenesis and in physical factors, will be added as funds and additional manpower become available.

The increase of $955,000 contains a program increase of $868,000 which will permit expansion of the Institute's principal research program primarily in the areas of environmental mutagenesis and reproductive toxicology and etiology of environmental diseases and disorders. Included in the increase is $25,000 for within-grade pay increases; $2,000 for BEC rate increase; $10,000 for increased utilities cost; $10,000 for an extra day of pay in 1975; $42,000 for the annualization of the 1974 pay raise; $8,000 for the Wage Board pay raise and $75,000 to the National Institutes of Health Management Fund. The increase is offset by a $85,000 employment savings reduction.

Research Management and Program Services

Authorizing Legislation: Public Health Service Act, Title III, Part A

	1974* Base		1975		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits.......	38	$756,000	38	$771,000	0	+$15,000
Other expenses.......	---	623,000	---	611,000	---	-12,000
Total.............	38	1,379,000	38	1,382,000	0	+3,000

Introduction

This activity supports the Office of the Director and the Office of the Associate Director for Extramural Programs and provides for the overall administration, coordination, and direction of the varied programs and activities of the Institute. The Office of the Director provides for the planning, direction, management, and coordination of all Institute activities; the review of current and proposed programs; the introduction of new knowledge into currently operating programs; and the provision and supervision of centralized administrative services. The Office of the Associate Director for Extramural Programs is responsible for the scientific and administrative management of the Institute's grants program. This includes the review and evaluation of research, fellowship and training grant applications for presentation to the Institute's Advisory Committees, and liaison with applicants, grantees, advisory bodies, other components of the National Institutes of Health and the Department of Health, Education, and Welfare, and other interested organizations.

Program Plans for 1974 and 1975

The Office of the Director will continue to devote most of its resources to the selection of the research questions which most need investigation and to the planning and direction of the total programs of the Institute. In addition, the Director serves as the American Coordinator of the Environmental Health Sciences portion of the US-USSR Health Agreement. Exchanges of scientists under this agreement have begun and will continue in 1975. The Director also serves as Project Chairman of the US-USSR Working Group on the Biological and Genetic Effects of Pollutants.

The net increase of $3,000 over the 1974 base includes a $5,000 requirement for within-grade pay increases, $2,000 for one extra day of pay in 1975, and $8,000 for the annualization of the 1974 pay raise. This is partially offset by a $12,000 reduction for the National Institutes of Health Management Fund.

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* Excludes 1973 appropriation restorations.

NATIONAL INSTITUTES OF HEALTH

National Institute of Environmental Health Sciences

Program Purposes and Accomplishments

Activity: Environmental Health Sciences Centers
(Public Health Service Act, Title III, Part A)

1974			1975 Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
---	$4,000,000	Indefinite	---	$5,100,000

Purpose: The University-based Centers were created to integrate the efforts of scientists in several traditional disciplines and foster application of expertise across disciplinary lines to environmental health problems.

Explanation: Because of the variety and complexity of environmental problems, several Centers with complementary spheres of interest are required to fulfill the national need. Accordingly, six Centers, each with special expertise in one or more of the major categorical programs of the Institute, were supported in FY 1974. Collectively, they provide outstanding capabilities in traditional basic and applied disciplines vital to the Institute program. The Centers are characteristically made up of groups of scientists who collaborate to develop fundamental and practical information about the causes and nature of environmental diseases in order to guide corrective and therapeutic programs. Their areas of expertise include, among others, chemistry, cell biology, genetics, physiology, biostatistics, pharmacology, toxicology, pathology, epidemiology, behavioral sciences, nutritional science, occupational medicine, and chemical and environmental engineering.

Accomplishments in 1974. Each of the Centers have made important contributions to the objectives of the Institute. Their studies deal with a wide variety of hazardous agents in the environment, the immediate focal points of public concern, and with specific diseases and disorders of environmental origin. Advances are being made in the identification and characterization of the sources, modes of entry, sites and basis of cell and tissue damage, and persistence of known and potential noxious agents. Important new data and insights are being developed regarding specific environmentally-related health problems, including chemical carcinogenesis; teratogenesis, and other reproductive disorders; neural and behavioral anomalies; respiratory, circulatory, and kidney diseases; and fundamental aspects of toxicant metabolism and disruptive interactions at the molecular and cellular levels. Further advances are being made in long-term population studies with emphasis on chemical epidemiology and on methodology for detecting early symptoms of fibrotic diseases of the lung, emphysema, and other disorders associated with occupational or accidental exposure to environmental chemicals and dusts.

Objectives for 1975: The budget request provides for funds to continue support of the 6 Centers funded in 1974 and for an additional Center for 1975. This additional Center has outstanding expertise in the chemistry and hazards of mercurials and other heavy metals and research capabilities to bring this expertise to bear on the categorical program interests and responsibilities of the Institute.

NATIONAL INSTITUTES OF HEALTH

National Institute of Environmental Health Sciences

Program Purposes and Accomplishments

Activity: Environmental Mutagenesis and Reproductive Toxicology
(Public Health Service Act, Title III, Part A)

1974			1975 Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
—	$2,150,000	Indefinite	—	$2,800,000

Purpose: This program aims at clarification of the nature and structure-activity relations of chemical agents capable of altering the genetic makeup of man, his reproductive capability, and in the development of the embryo or fetus. A further aim is to develop mutagenicity test systems with unequivocal quantitative relevance to man.

Explanation: A major effort in this program is being made in the Institute's laboratories. However, this is supplemented to a considerable degree through individual, Program and Center grants. The studies will provide an understanding of the molecular basis for visible changes in biochemistry and morphology due to mutagenic and teratogenic agents. Efforts are being made also to assess existing mutagenesis test procedures for relevance to man and toward development of new procedures. This is a high priority aspect of the program. Serious deficiencies in present test systems must be bridged to facilitate progress toward assessment of environmental agents, food additives and natural products for mutagenic potential in man.

Accomplishments in 1974: Progress is being made toward further understanding of the chemistry of molecular interactions between DNA and mutagenic agents such as cyclamates, saccharin, azides, nitroso compounds, nitrites and PCBs. Studies in reproductive toxicology range from efforts to establish etiological relationships between toxicants and specific disorders to those designed to elucidate the molecular and cellular basis of teratogenesis and hormone changes. The agents of primary concern are widespread compounds such as chlorinated hydrocarbon and organophosphate insecticides, fungal metabolites, dioxins, mercurials and a number of pharmaceuticals and industrial intermediates.

In the case of PCBs, it was found that though the compounds have no effects on genes or reproduction during the first generation after exposure, continued exposure over several generations results in chromosomal damage and birth defects. This study points up the necessity for long-term, multigeneration testing and the possible need to reassess present standards for setting long-term tolerances of potential mutagens. Other studies have shed further light upon the gestational period during which the fetus is at maximum risk and on the nature of anomalies induced by exposure to specific times during fetal development.

Objectives for 1975: The budget request provides for continued research on environmental compounds as they influence man's genetic makeup, his reproductive capability, and the healthy development of future generations.

NATIONAL INSTITUTES OF HEALTH

National Institute of Environmental Health Sciences

Program Purposes and Accomplishments

Activity: Etiology of Environmental Diseases and Disorders
(Public Health Service Act, Title III, Part A)

1974			1975	
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
---	$4,385,000	Indefinite	---	$4,100,000

Purpose: The central objective of the etiology program is to establish causal associations between human diseases and noxious chemical and physical factors in the environment. This involves description and characterization of pathological lesions and endpoints in specific target organs and inter-dependent physiological systems.

Explanation: This program is carried out both by the intramural staff and through grants and contracts. Thousands of new chemicals are synthesized each year. Many of these are brought into production, adding to the thousands already in use in industry to make home and personal care products, food and fuel additives, pesticide and pharmaceutical preparations, and a host of others. Despite increased efforts by manufacturers and government agencies to test new and existing compounds, the biological effects of many of these substances alone and in combinations are still unknown. The research is designed to provide a sound basis for clinical recognition of environmentally-related disorders of man and their causes and for implementation of correct therapeutic and preventive measures. In a broader sense, its aim is to provide a foundation for wise management of current technology and future industrial development in order to make them compatible with human health and well-being.

Accomplishments in 1974: Evidence was obtained that several widely used pesticides disrupt nerve function and may influence behavioral and learning patterns. Further probing of the long-term effects of lead and mercury on the central and peripheral nervous systems reveals adverse effects on learning and behavior even before visible damage to the nervous system is evident. These studies add a new dimension to problems of detection of cause-effect relations. New toxins were detected in fungi often associated with grains and other food staples. The different toxins cause a variety of syndromes ranging from carcinoma and edema of the lungs to photosensitization and neurological and kidney damage. Advances are being made in understanding the influence of heat stress, light, noise, microwaves and laser radiation on physiological systems. New insights are being developed into disorders of the lungs and cardiovascular systems induced by ozone, oxides or nitrogen and sulfur, and by industrial dusts from coal, plastics, asbestos, textiles and others. Epidemiological studies provide evidence that cancer, fibrotic diseases, emphysema and bronchitis is often greatly enhanced by cigarette smoking and inhalation of lung irritants characteristic of urban atmospheres. These findings emphasize the need for further intensive studies on the etiology of environmental diseases.

Objectives for 1975: The budget request provides for additional research on chemical, physical and biological agents in the environment that may act, singly or in combination, as progenitors of human disease.

NATIONAL INSTITUTES OF HEALTH

National Institute of Environmental Health Sciences

Program Purposes and Accomplishments

Activity: Environmental Pharmacology and Toxicology
(Public Health Service Act, Title III, Part A)

1974		1975		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
---	$5,881,000	Indefinite	---	$4,334,000

Purpose: The pharmacology-toxicology program is designed to develop understanding of the principles and mechanisms involved in the toxicity of environmental agents. Its further aim is to characterize the nature and sites of molecular, cellular and tissue interactions with toxicants and to relate these to functional disorders.

Explanation: These studies are carried out both within the Institute's laboratories and through individual grants and contracts and Program and Center grants. Work in several laboratories focuses on the nature and basic mechanisms of chemical transformations of environmental agents in the environment and in the body. A major segment of the program deals with inherent defense systems such as binding, exclusion, storage, metabolic and clearance systems. Substantial effort is devoted also to clarification of interactions between specific enzymes and metabolic targets responsible for gross manifestations of toxicity. The goal is to provide a rational basis for maintaining, through environmental management, reasonable safety margins between environmental and body burdens of toxic agents in order to safeguard human health now and in future generations.

Accomplishments in 1974: Ongoing work shows that many noxious compounds are susceptible to transformation by visible and ultraviolet radiation and other factors in the environment and by various enzymes in the body. Continuing studies indicate that aromatic petroleum products, common as air pollutants, can give rise to carcinogenic agents. Several pesticides, particularly aldrin and dieldrin, are converted to more toxic derivatives on exposure to sunlight. These findings will facilitate understanding of toxicity mechanisms. The mode of several toxic metals were studied and new causal relations in lead and mercury toxicity were found. The nature of drug metabolizing enzymes and their roles in transformation of toxic chemicals, in body clearance, and in activation of carcinogenic agents were clarified in large part. Parallel advances are being made in analytical methodology for dioxin, a contaminant in the manufacture of 2,4,5-T herbicide, which is the most toxic and teratogenic synthetic compound known. The methodology has broad application for chlorinated compounds. These accomplishments and others constitute a substantial stride toward establishing the risk-benefit equation in the massive use of chemicals, upon which modern technology is heavily dependent.

Objectives for 1975: The budget request provides for continued pharmacological and toxicological studies of environmental agents as they enter the body, are distributed, and as they disrupt the normal functions and structures of the body.

NATIONAL INSTITUTES OF HEALTH

National Institute of Environmental Health Sciences

Program Purpose and Accomplishments

Activity: Environmental Pathogenesis (Public Health Service Act, Title III, Part A)

1974		1975		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
---	$2,340,000	Indefinite	---	$1,810,000

Purpose: The pathogenesis program deals with the details and time sequence of molecular and cellular events that culminate in recognizable diseases and other endpoints upon exposure of individuals to toxic agents.

Explanation: This work is carried out both in intramural laboratories and through grants and contracts. Because of the wide range of chemical and physical factors present in the environment, no organ or body function can be considered invulnerable to damage by environmental agents. Diseases of the pulmonary and cardiovascular systems, the liver, kidneys, reproductive system, and degenerative disorders of long-term and complex etiology have been well documented and related to environmental factors. The program is designed to develop knowledge of initial or very early molecular and cellular lesions that will facilitate implementation and improve the effectiveness of prophylactic or therapeutic measures before damage in target organs becomes irreversible and progressive.

Accomplishments in 1974: Studies on the biologic effects of radiation led to the development of new lighting systems that closely simulate noon sunlight. This has permitted critical experiments that have shed new light on phototoxic reactions, light-induced cancer, and potentiation of these effects by chemical agents. Studies on the process of transition of normal into cancerous cells have added new insight into the phenomena associated with cancer. The evidence suggests that cancer formation involves at least three steps. The first step is called initiation, and probably involves a somatic mutation. The second step is promotion which involves uncontrolled cell division. The third step is a phase of rapid cell growth. Several environmental agents which bring about the first two steps have been identified and chemically characterized.

Further insight is being provided into the lesions caused by lead and mercury in the peripheral and central nervous systems. Damage to the sheath in nerve fibers and damage to structures constituting the blood-brain barrier provide understanding of lead brain damage which is common in lead-poisoned children, and of persistent changes in learning and behavioral patterns of such children. The basis of lung fibrosis from exposure to agents such as beryllium and asbestos has been clarified in large part through studies of immunology. The relationship between cancer and other diseases of the lung and industrial dusts and irritant gases have been considerably illuminated through basic studies of inhibition of lung defense mechanisms.

Objectives for 1975: The budget request provides for further research on the initial or very early molecular and cellular lesions that lead to human environmental diseases or the complication of pre-existing health problems.

NATIONAL INSTITUTES OF HEALTH

National Institute of Environmental Health Sciences

Program Purposes and Accomplishments

Activity: Intramural Laboratory and Clinical Research
(Public Health Service Act, Title III, Part A)

1974			1975	
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
197	$8,203,000	Indefinite	197	$9,158,000

Purpose: The intramural research program was created for the purpose of investigating at the fundamental level the long term overt and subtle effects of chemical and physical environmental factors potentially hazardous to man, without limitations regarding the origin or sources of such factors.

Explanation: The laboratory and clinical research program consists of six branches concerned with directed fundamental research. Three of these have additional responsibilities for research support. The overall goal is to develop a reliable data base for use in establishing standards and devising remedial measures in a variety of populations at risk from exposure to environmental and occupational chemicals and physical factors. The programs focus especially on toxicology and pharmacology, reproductive biology, mutagenesis and pathology. Support in synthetic and analytical chemistry, in biomedical instrumentation design and development, in computer technology, and administrative and clerical services are provided.

Accomplishments in 1974: Considerable effort has been devoted to development of basic information regarding the sites and mode of action of heavy metals. Notable advancements are being made in understanding of the biochemical and structural basis of neurological and teratogenic effects of lead and mercury. Progress is being made toward elucidation of structure-activity relations, metabolism, pharmacodynamics, mechanisms of action and mechanisms of detoxication and toxicity enhancement of pesticides. New light has been shed on the role of individual compounds and combinations of factors in birth defects, reproductive disorders and carcinogenesis. Efforts in mutagenesis research are being intensified, with development of new insight into the nature of mutagens, their sites and modes of interaction with DNA, and their effects of DNA repair systems. Refinements are being made in the host mediated assay and other test systems for mutagenicity. Work has been expanded and progress is being made toward establishing quantitative relationships between biological effects and physical factors such as noise, microwaves and radiation. In addition to the indicated research activities, the administrative and staff organize and sponsor workshops and conferences for synthesizing information on specific subjects and assessing the state of the art in several areas of vital concern to the Institute.

Objectives for 1975: The total increase of $955,000 contains $87,000 for built-in requirements and $868,000 for a program increase. This increase would permit the expansion of our intramural research program in the areas of environmental mutagenesis and reproductive toxicology, and etiology of environmental diseases and disorders.

NATIONAL INSTITUTES OF HEALTH

National Institute of Environmental Health Sciences

Program Purposes and Accomplishments

Activity: Research Management and Program Services
(Public Health Service Act, Title III, Part A)

1974			1975 Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
38	$1,379,000	Indefinite	38	$1,382,000

Purpose: This activity supports the Office of the Director and the Office of the Associate Director for Extramural Programs and provides for the overall administration, coordination, and direction of the varied programs and activities of the Institute.

Explanation: The Office of the Director provides for the planning, direction, management, and coordination of all Institute activities; the review of current and proposed programs; the introduction of new knowledge into currently operating programs; and the provision and supervison of centralized administrative services. The Office of the Associate Director for Extramural Programs is responsible for the scientific and administrative management of the Institute's grants program. This includes the review and evaluation of research, fellowships and training grant applications for presentation to the Institute's Advisory Committees and liaison with applicants, grantees, advisory bodies, other components of the National Institutes of Health and the Department of Health, Education, and Welfare, and other interested organizations.

Accomplishments in 1974: During 1974, the Office of the Director devoted a significant portion of its resources to the selection of the research questions which most need investigation and to the planning and direction of the total programs of the Institute. In addition, the Director serves as the American Coordinator of the Environmental Health Sciences portion of the US-USSR Health Agreement. Exchange of scientists under this agreement have begun and will continue in 1975. The Director also serves as Project Chairman of the US-USSR Working Group on the Biological and Genetic Effects of Pollutants. The Extramural program staff advanced its effort to strengthen its liaison and management activities in order to obtain maximum benefits from the available grant funds.

Objectives for 1975: The Office of the Director will continue to devote most of its resources to the selection and assignment of priorities to research questions and to the planning and direction of the Institute's programs. The Extramural program staff will maintain surveillance over approximately 250 grants and awards anticipated to be funded during this year.

Tuesday, April 2, 1974.

NATIONAL EYE INSTITUTE

WITNESSES

DR. CARL KUPFER, DIRECTOR
DR. ROBERT S. STONE, DIRECTOR, NATIONAL INSTITUTES OF HEALTH
DR. DeWITT STETTEN, JR., DEPUTY DIRECTOR FOR SCIENCE, NATIONAL INSTITUTES OF HEALTH
DR. GEORGE T. BROOKS, ASSOCIATE DIRECTOR, NATIONAL EYE INSTITUTE
EDWARD H. McMANUS, EXECUTIVE OFFICER, NATIONAL EYE INSTITUTE
KENNETH O. COOKE, BUDGET OFFICER, NATIONAL EYE INSTITUTE
LEON M. SCHWARTZ, ASSOCIATE DIRECTOR FOR ADMINISTRATION, NATIONAL INSTITUTES OF HEALTH
LELAND B. MAY, ACTING DIRECTOR OF FINANCIAL MANAGEMENT, NATIONAL INSTITUTES OF HEALTH
CHARLES MILLER, DEPUTY ASSISTANT SECRETARY, BUDGET

Object Classification (in thousands of dollars)

Identification code 09-25-0887-0-1-651		1973 actual	1974 est.	1975 est.
	Direct obligations:			
	Personnel compensation:			
11.1	Permanent positions	1,882	2,053	2,071
11.3	Positions other than permanent	117	113	120
11.5	Other personnel compensation	47	33	35
	Total personnel compensation	2,046	2,199	2,226
12.1	Personnel benefits: Civilian	213	260	268
21.0	Travel and transportation of persons	92	129	160
22.0	Transportation of things	6	10	20
23.0	Rent, communications, and utilities	91	65	95
24.0	Printing and reproduction	41	13	44
25.0	Other services	4,566	5,688	5,644
26.0	Supplies and materials	244	243	353
31.0	Equipment	445	232	431
41.0	Grants, subsidies, and contributions	26,645	35,264	30,706
	Total direct obligations	34,389	44,103	39,947
	Reimbursable obligations:			
21.0	Travel and transportation of persons	2		
99.0	Total obligations	34,391	44,103	39,947

Personnel Summary

Total number of permanent positions	134	128	129
Full-time equivalent of other positions	8	8	8
Average paid employment	123	123	123
Average GS grade	8.5	8.6	8.6
Average GS salary	$14,260	$15,138	$15,473
Average salary of ungraded positions	$11,138	$12,018	$12,253

Program and Financing (in thousands of dollars)

	Identification code 09–25–0887–0–1–651	1973 actual	1974 est.	1975 est.
	Program by activities:			
	Direct program:			
	1. Retinal and choroidal diseases	13,316	14,098	12,534
	2. Corneal diseases	5,561	6,851	6,039
	3. Cataract	2,745	3,474	2,987
	4. Glaucoma	4,073	5,097	4,496
	5. Sensory-motor disorders and rehabilitation	7,319	8,341	7,459
	6. Intramural laboratory and clinical research	4,124	4,323	4,458
	7. Research management and program services	1,933	1,919	1,974
	Total direct program	39,071	44,103	39,947
	Reimbursable program:			
	7. Research management and program services	2	---------	---------
	Total program costs, funded[1]	39,073	44,103	39,947
	Change in selected resources (undelivered orders)	–4,682	---------	---------
10	Total obligations	34,391	44,103	39,947
	Financing:			
14	Receipts and reimbursements from: Non-Federal sources	–2	---------	---------
25	Unobligated balance lapsing	4,181	---------	---------
	Unobligated balance restored	---------	–4,165	---------
	Budget authority	**38,570**	**39,938**	**39,947**
	Budget authority:			
40	Appropriation	38,562	41,631	39,947
	Withheld from obligation and expenditure (Public Law 93–192)	---------	–1,684	---------
41	Transferred to other accounts	---------	–9	---------
42	Transferred from other accounts	8	---------	---------
43	**Appropriation (adjusted)**	**38,570**	**39,938**	**39,947**

[1] Includes capital outlay as follows: 1973, $700 thousand; 1974, $323 thousand; 1975, $392 thousand.

		1973 actual	1974 est.	1975 est.
	Relation of obligations to outlays:			
71	Obligations incurred, net	34,391	44,103	39,947
72	Obligated balance, start of year	26,182	26,228	34,144
74	Obligated balance, end of year	–26,228	–34,144	–35,506
77	Adjustments in expired accounts	–20	---------	---------
90	Outlays	34,325	36,187	38,585

NOTES

Includes $70 thousand in 1975 for activities previously financed from: National Institute of General Medical Sciences, 1973, $60 thousand; 1974, $60 thousand.

Excludes $9 thousand in 1974 and 1975 for activities transferred to Departmental Management. Comparable amount for 1973 ($9 thousand) is included above.

Mr. **Flood**. The committee will come to order.

WITNESS INTRODUCTION

We now have the National Eye Institute. I see we have with us Dr. Carl Kupfer, the Director of the National Eye Institute.

We will place in the record your biographical sketch, Doctor.

[The biographical sketch follows:]

Biographical Sketch

Name: Carl Kupfer, M.D.

Position: Director, National Eye Institute.

Birthplace and date: New York, N.Y., February 9, 1928.

Education: A.B., Yale University, 1948; M.D., the Johns Hopkins Medical School, 1952.

Experience present: Director, National Eye Institute, National Institutes of Health.

1966–70: Professor and Chairman in Ophthalmology, University of Washington School of Medicine.

1962–66: Assistant Professor in Ophthalmology, Harvard Medical School.

1960–62: Instructor in Ophthalmology, Harvard Medical School.

1958–60: Research Fellow in Ophthalmology, Harvard Medical School.

1957–58: Research Fellow in Ophthalmology, Wilmer Eye Institute, the Johns Hopkins Medical School; Laboratory Assistant, Biostatistics, the Johns Hopkins Medical School.

1953–54: Laboratory Assistant, Biostatistics, the Johns Hopkins Medical School.

1952–54: Internship and Assistant Residency, Wilmer Eye Institute, the Johns Hopkins Hospital.

Association memberships: American Physiological Society; Association for Research in Vision and Ophthalmology; American Academy of Ophthalmology and Otolaryngology; American Ophthalmological Society.

Publications: Author or coauthor of approximately 40 publications in clinical ophthalmology and the anatomy, physiology and biochemistry of the visual system.

Mr. **Flood**. I see you have a prepared statement. How do you want to proceed?

Dr. **Kupfer**. I would like to present it, if I may.

Before I do, I would like to introduce Mr. Edward McManus, the Executive Officer, and Dr. George Brooks, the Associate Director of Extramural and Collaborative Programs at the National Eye Institute.

Opening Statement

Mr. Chairman and members of the committee, eye diseases constitute one of the most serious causes of suffering and disability in our Nation today. An estimated 9.6 million people in the Uinted States are visually impaired. Fourteen percent of these cannot read newsprint with either eye, even with glasses. At least 32,000 people in our country become blind every year, and most will require financial assistance from governmental and private agencies, as well as other special services, in order to live out their lives with some degree of dignity and comfort.

In the face of the great progress which research has made possible in eye care during the last two decades, it must be explained why we still face such serious problems. For the new treatments and cures developed during this period have been truly remarkable. Cataract surgery, once difficult, risky, and uncomfortable to the patient, has evolved into one of the safest, most successful, and least painful of any major surgical procedure. Retinal detachment, a nearly hopeless condition several years ago, is now reparable in the great majority of cases if treated early. An array of drugs has been developed to control chronic glaucoma, and surgery can now cure acute glaucoma, thereby reducing the incidence of blindness caused by these diseases. Newer breakthroughs, such as the use of soft contact lenses to treat diseases of the cornea, and surgical instruments which enable safe operation on the vitreous, the clear jelly-like tissue in front of the retina, are reducing suffering and restoring sight to those who were without hope just a short time ago.

Yet, despite these accomplishments, eye disorders continue to take their high toll. Over 3 million people have some visual disability due to cataract, and over 800,000 have glaucoma. Of the estimated 340,000 blind people in the United States, retinal diseases are responsible for nearly 40 percent, and thousands are, today, slowly losing their sight from this cause. Among those chronic diseases which restrict the ability of Americans to lead productive lives—that is carry out such major activities as working or going to school—visual impairment ranks third, after heart disease and arthritis.

The only hope for significantly diminishing these statistics is continued laboratory and clinical biomedical research. Research has enabled us to progress this far, and it is only through additional research that the ultimate prevention of eye diseases will be achieved. For any real major impact on cataract and glaucoma, means of preventing these diseases must be found. For retinal disorders, the development of treatments and cures—where none now exist—would, of course, be highly beneficial. But the discovery of ways to prevent these disorders as well would be even more rewarding. An example of research leading to the prevention of a serious eye disease is the case of retrolental fibroplasia, which is well-known to members of this committee.

CATARACT

Cataract is a particularly apt illustration of a field of eye research in which major emphasis must now be placed on prevention. New developments in surgery and improved postoperative management of patients suggest that the length of hospitalization required following cataract removal may only be a day or two. However, cataract surgery, no matter how streamlined or improved, is not a cure for this disease. Because cataract surgery involves removing the natural lens of the eye, a substitute, in the form of thick eyeglasses or contact lenses, must be provided. This is not an ideal solution because, although good visual acuity may be restored, loss of side vision and magnification of image size are common consequences—ones to which many patients find it difficult to adjust. Even more to the point is the fact that, despite the availability of sophisticated surgical methods and the large number of operations performed each year (approximately 400,000 at a total estimated cost of $1 billion annually), cataract still remains a major cause of blindness in the United States. This is partly the case because some people with cataract are afraid to undergo surgery and others are not able to afford the cost of treatment. But, whatever the reason, the fact is that a large number of people do not have their cataracts removed, and it is possible that no amount of health education, further surgical breakthrough, or additional financial assistance will have a significant impact on remedying this situation. But, if a means of prevention were at hand, disability, financial burden, and lost productivity could be minimized and human suffering greatly alleviated.

Last year I told the committee about a cataract research workshop which we planned to convene. This was held late in October. Leading scientists in this field met at NIH to pool their knowledge and ideas for the future direction of cataract studies. Their report, which will soon be published, highlights significantly new developments in laboratory and clinical research, outlines the main opportunities and needs in this field, and points the way toward additional studies which are required to attain the means of preventing or retarding the development of cataract.

The committee may recall that in previous testimony I have reported on the progress which has been made in the prevention of sugar cataracts in laboratory animals and in testing new theories on the formation of senile cataract in humans. As a result of these studies, additional investigations are now underway which hold great promise for resulting in important new discoveries related to cataract prevention within the near future.

We expect that the cataract workshop and its report will have a great impact on the future of cataract research and will serve to attract new investigators to a field in which, at present, only a relatively few dedicated men and women are working.

RETINAL DISEASES

Many people, I have found, are surprised to learn that diseases of the retina—in particular senile macular degeneration and diabetic retinopathy—are responsible for more blindness and visual disability than any other cause. As a group, retinal diseases are the most difficult of eye disorders for, with the exception of retinal detachment, little can be done to prevent or treat them. Even diagnosis may be a problem because of the relative inaccessability of the retina and the similar appearance of many retinal diseases, the causes of which are not known. In a recently published survey conducted by Research to Prevent Blindness, Inc., a group of practicing ophthalmologists rated retinal diseases, particularly retinal degeneration and diabetic retinopathy, as the most difficult eye disorders to treat. They also considered retinal diseases as those in most need of further research. After cataract, retinal diseases were rated as the most frequently seen disease in the ophthalmologists' practice.

Research offers hope for progress against retinal disease. What is needed most is more fundamental knowledge of how the normal retina functions. The complex chemical and physical interactions between light and living tissues are only partially understood. Much more must be learned about what goes wrong when the retina ceases to function normally and breaks down. Clinical studies of retinal diseases are needed as well. But they are impeded by the lack of basic information.

A considerable amount of excellent work has been and is being done to provide the foundation upon which targeted programs against retinal diseases will one day be based. But it is important to emphasize the magnitude of this task. The retina—a fragile tissue only one-fiftieth of an inch thick and the size of an ordinary postage stamp—contains approximately 125 million light-sensitive photoreceptor cells, as well as other structures which, taken as a whole, rivals the brain in anatomical and functional complexity.

During the past year, NEI grantees reported their development of a new method of measuring ocular blood flow using microscopic radioactive plastic spheres. This has provided a new and more reliable way of studying the alteration of blood flow to the retina which occurs in a number of diseases. Another accomplishment, made with NEI grant support, has been the use of a dye, indocyanine green, which enables visualization of the choroid, the blood vessel tissue which supplies nourishment to the retina. This technique allows, for the first time, differentiation between normal and abnormal blood circulation behind the retina.

In addition to research supported by grants, the Institute has used the contract to provide important resources for retinal research. Last year I reported on the successful development, under an NEI contract, of an automated biomedical image processor for the study and analysis of nerve tissue. Recently, as a result of another NEI contract, breeding pairs of a strain of rats with an inherited form of retinal degeneration are being made available free of charge to qualified investigators. The rats have a condition which is strikingly similar to certain retinal diseases in humans, in particular retinitis pigmentosa, a form of peripheral retina degeneration which leads to partial or total blindness by adolescence or early adulthood. It is our hope that by making these experimental animals widely available to the research community, more will be learned about the mechanisms underlying degenerative diseases of the retina.

GLAUCOMA

In previous years I have also told the committee about new developments in the diagnosis and treatment of glaucoma. I can now report another advance in this field, one in which I have been personally involved. In studies conducted in the NEI clinical branch, we have been able to produce a condition in the eyes of Rhesus monkeys which appears to be very similar to human, chronic open-angle glaucoma. This is the closest we have yet come to producing an animal model of this disease. Again, this will provide the research community a new investigative tool which we hope will be useful in the development of new methods of glaucoma treatment and lead to a better understanding of how elevated pressure within the eye can lead to damage to the optic nerve.

In another area of glaucoma research, new studies have borne out the early promise of the use of a new drug—6-hydroxydopamine—which I reported last year could greatly enhance the pressure lowering effect of epinephrine, a drug now widely being used for the treatment of glaucoma. After 2 years of study this drug has proven safe and effective in controlling the intraocular pressure of many patients who had not been helped by epinephrine alone or by glaucoma surgery. Many patients who could not tolerate high dosages of glaucoma drugs, or those with far advanced disease, have been greatly benefited by this mode of treatment. It will, we hope, become an important adjunct to conventional glaucoma therapy.

CORNEAL DISEASE

Diseases of the cornea account for approximately 6 percent of blindness but have a much greater impact in terms of their contribution to reduced visual acuity and suffering, for they are the most painful of eye disorders. The cornea is that part of the eye most vulnerable to accidental injury. Infectious and degenerative diseases of this tissue are often difficult to cure.

NEI grantees recently demonstrated that the shape of the cornea can be safely remolded by controlled levels of heat, offering new hope for victims of keratoconus, a condition in which the center of the cornea becomes conical in shape, causing reduced vision. The technique may also be useful for correcting severe cases of nearsightedness and other optical conditions.

The development of an experimental treatment for donor corneas to inhibit their rejection as corneal transplants was also reported by Institute-supported investigators. This treatment provides a possible basis for protecting the transplanted tissue without use of potentially dangerous immunosuppressive drugs.

An Institute-convened task force on corneal disease published its reported in June and ranked studies of immunology, herpes simplex viral infections, opacification, and edema as among the highest priorities for corneal disease research. At the present time, these areas are receiving major emphasis in the Institute's corneal research program.

Finally, I would like to describe one of the major management efforts now being undertaken by the Institute. A subcommittee of our Advisory Council has been appointed to advise the Institute whether there is appropriate distribution of resources within and between our programs. Expert consultants from the research community have also been asked to assist the Council in this project.

We have recently completed a detailed review and analysis of our Retinal and Choroidal Disease program and find that, in general, the distribution here is good. However, two general conclusions reached are that more clinical research needs to be stimulated and additional basic laboratory work, emphasizing prevention of retinal diseases, needs to be undertaken.

In summary, to carry out the program I have discussed today as well as other Institute programs designed to translate research results into clinical application, and toward the alleviation of blindness and visual disability, the National Eye Institute's budget request for fiscal year 1975 is $39,947,000.

I shall be pleased to answer any questions and supply additional information the committee may desire for the record.

CATARACT

Mr. Flood. Doctor, down through the years whenever we hear the word "cataract" the first thought is surgery. Nobody ever heard of anything else as long as I can remember.

Is surgery the only method of treatment of cataracts? Somebody has a cataract and there it is. Regardless of whether it is a senile cataract or sugar cataract, there is the cataract.

By the way, you might tell us the difference between the types and kind of cataracts. What about that?

Dr. KUPFER. Yes, sir. One might say there are three types of cataracts. The first and the most common is senile cataract.

Mr. FLOOD. What does that mean?

Dr. KUPFER. First of all, a cataract is an opacification of the lens in the eye.

Mr. FLOOD. By that you mean opaque?

Dr. KUPFER. Yes, sir. Ordinarily, the lens in the eye is crystal clear to allow light to pass through and come to focus on the retina, the seeing part of the eye. If the lens becomes opaque, the light can't reach the retina. This is called a cataract.

Mr. FLOOD. What gave birth to the term—something that falls down?

Dr. KUPFER. Yes, sir. This cataract accounts for the majority of cataracts and occurs in people in their sixties, seventies, and eighties.

The second type of cataract which clinically is very important is the congenital or developmental cataract. This is the cataract occurring in infants and children. This constitutes a significant cause of cataracts and is particularly important because removal of the cataract surgically in an infant disrupts the eye enough so that many years later other eye diseases may intervene.

Mr. FLOOD. So the cataract is not a thing or condition which exists only in those of advanced age?

Dr. KUPFER. No, sir.

There is a third type of cataract that includes sugar cataract which is the cataract associated with diabetes, cataract caused by X-radiation, or conditions where the calcium balance in the blood is not appropriate.

Mr. FLOOD. What about trauma?

Dr. KUPFER. Trauma can certainly cause cataracts also. We would put these in the third group. It is in this group that the major research efforts have been directed and successfully completed, now that researchers are beginning to turn their attention to senile cataracts and congenital cataracts.

CATARACT TREATMENT

Mr. FLOOD. Is surgery the only method of treatment of the cataracts?

Dr. KUPFER. At the present time surgery is the only method of treatment.

Mr. FLOOD. Are there any other methods of treatment you have under investigation, any breakthroughs by anyone?

Dr. KUPFER. There has been a breakthrough as a matter of fact. In the case of cataracts caused by diabetes, if one produces diabetes in an experimental animal——

Mr. FLOOD. What is diabetes generally?

Dr. KUPFER. The basic problem is inability of the body to regulate the level of sugar in the blood.

Mr. FLOOD. What about the opposite of too much sugar, too little sugar?

Dr. KUPFER. Too little sugar would be a condition that also occurs clinically.

Mr. FLOOD. Which could also produce the condition?

Dr. KUPFER. Not usually, sir. It is too much sugar that produces the cataracts although in infants with hypoglycemia—low blood sugar—a rare form of cataract may occur. This type of condition in an experimental animal now can be slowed down considerably by the use of eye drops. I think this really represents a very significant breakthrough.

Mr. Flood. What about treatments other than surgery then, for either of the conditions?

Dr. Kupfer. At the present time there is evidence from the laboratory that the type of cataract caused by diabetes could be slowed down by medical treatment. We have yet to test this clinically. I think this would be one of the next steps to become involved in.

Mr. Flood. You are attacking the sugar rather than the physiology of the eye I suppose.

Dr. Kupfer. We are attacking the problem that exists in the lens when it is confronted with a very high level of sugar. Ordinarily the lens takes in the sugar and converts the sugar into something which then interferes with the normal lens function.

Mr. Flood. I suppose you tell physicians any time you find someone with diabetes you had better start preventing cataracts at the same time, if they don't know it.

Dr. Kupfer. I think the general medical community is aware of the complication of the cataract in diabetes. I would say in the next 5 or 10 years we will perhaps have some studies in patients that will tell us whether we can slow down the cause of cataracts in diabetics.

Mr. Flood. How do you slow down the treatment of senile cataracts?

Dr. Kupfer. To date we don't have any approach to this problem. We have some ideas which are being tested in the laboratory and I think these are promising, as I mentioned last year.

Mr. Flood. You can't stop people from getting older, can you?

Dr. Kupfer. No, sir.

Mr. Flood. Your statement suggests that we are on the verge of finding a way to prevent cataracts, a prophylactic kind of thing. Can you be more specific about that? What do you have in mind?

Dr. Kupfer. Perhaps we should go back to the sugar cataract situation again, the cataract that occurs in diabetics. As diabetics, like anyone else become older, they undergo the changes of senile cataracts, and it appears that the presence of the diabetes accelerated this senile change. There is also a rare form of cataract found in young people with diabetes. If we could control the effects of the high sugar on the lens, there is a definite possibility we would slow down the rate at which they would develop a cataract. In fact, this would never interfere with their vision. I think it is this approach that will be tested in the next 5 years.

CATARACT WORKSHOP

Mr. Flood. Last year you mentioned the cataract research workshop.

Dr. Kupfer. Yes, sir.

Mr. Flood. Apparently that outlined the main opportunities that you have for the needs in this field. Does this 1975 budget address those specific opportunities and needs that were generated by the workshop in October?

Dr. Kupfer. At the present time, we are spending approximately $3 million on cataract research. I think that this would include most of the opportunities that have been identified by this cataract workshop.

Mr. Flood. You say the report of the cataract workshop will serve to bring in new investigators in this field.

Dr. Kupfer. Yes, sir.

CATARACT RESEARCH

Mr. Flood. How can you attract new investigators into this field, with a stationary budget? Take a look at page 111 of your justifications. For 1974, $2,987,000; for 1975, $2,987,000. How do you do that?

Dr. Kupfer. I think one of the approaches is to establish some priorities in one's mind. We have begun with the advisory council in the area of retinal diseases to decide what are our highest priorities so we can make maximal use of the resources we have. I think we have to do the same thing in the cataract area also.

Mr. Flood. If you had additional money, would cataract research be the No. 1 priority?

Dr. Kupfer. I think it would be very high up. Certainly No. 1 or 2 in our priorities, sir.

Mr. Flood. How about the way you go about this, the mechanism you pursue in that kind of research. Would that be grants or contracts, intramural research?

Dr. Kupfer. At the present time, we do not have any contract support for cataract research per se. I think this would all be through the grant mechanism to individual investigators.

In addition, we probably do have one of the strongest cataract research units right in the Bethesda laboratories of the National Eye Institute. So there would be continued support of cataract research at our own institution.

Mr. Flood. With that record in front of us, are there any approved but unfunded research projects in the field of cataract research right now?

Dr. Kupfer. Yes, sir.

Mr. Flood. How many? There they are approved. So what? How many are there?

Dr. Kupfer. I can tell you that in 1974, this present fiscal year, we are funding approximately 35 to 40 percent of our approved grants. In the cataract area, we have a total of 35 grants, of which 12 are new awards, and it would be hard to know what further number have been approved but not funded. It would be a significant number, approximately additional 25 grants.

Mr. Flood. That is a lot, isn't it?

Dr. Kupfer. Yes, sir.

OPHTHALMOLOGIST TRAINING

Mr. Flood. Now, your plans for 1975 include "stressing the training of ophthalmologists in an environment that encourages exposure to the basic sciences." What does that mean?

Dr. Kupfer. In the case of cataract reesearch, perhaps even more so than in other research areas, the relationship between the clinician and the laboratory researcher is particularly important because it is the clinician who, at the present time, is removing the cataract surgically and who could make this material available to the biochemist or physiologists for study. If we are going to learn more about how the cataract becomes opaque, we have to study the tissue. This reciprocal relationship does not exist in as many institutions as we wish it did.

Mr. Flood. The basic scientist?

Dr. KUPFER. The clinician who does the surgery and is familiar with the clinical problem should be working hand in hand with the laboratory researcher who must look at the human situation.

Mr. FLOOD. How much of the money in the 1975 budget are you going to use for the training of ophthalmologists?

Dr. KUPFER. The present level for training grants for 1975 is approximately $2 million. I would say that about two-thirds of that will be used for the training of ophthalmologists. In addition there might be perhaps half the fellowship money which would be approximately another $1 million for the training of ophthalmologists. So we are talking about perhaps $2 million in toto.

Mr. FLOOD. How many trainees does that support, about?

TRAINING PROGRAMS

Dr. KUPFER. I would say in fiscal 1975 we would probably have about 40 or 50 training grants, because some of these training funds provide salaries for the preceptors who do the training.

Mr. FLOOD. How do those figures compare with 1972, 1973, and 1974?

Dr. KUPFER. They are much less.

Mr. FLOOD. Very, very, very much less?

Dr. KUPFER. I could give you the figures. In 1973 there were 107 individuals in training, in 1974 there were 123, and in 1975 it drops to 75.

Mr. FLOOD. Suppose you were sitting where I am and after the last 18 questions I have asked you and after listening to your statement out of the clear blue sky, I ask the last question and I get the last answer. What would you think?

Dr. KUPFER. I think that what I should do to make the picture complete is point out that in terms of the training grants, we are supporting fewer and fewer trainees, but in terms of fellowships we have gone from 57 in 1973 to 146 in 1974——

Mr. FLOOD. What is the difference between a training grant and fellowship?

Dr. KUPFER. The trainee is included under a training grant given to the Department and he would be a participant in an ongoing program. Fellowships are awarded to individuals to increase the number of teachers and scientists working full time in the visual sciences.

OPHTHALMOLOGISTS AND OPTOMETRISTS

Mr. FLOOD. How many ophthalmologists are there in the United States?

Dr. KUPFER. Approximately 10,500. sir. That includes all licensed ophthalmologists in the country, including those who are actively practicing as well as those who are retired.

Mr. FLOOD. How many should there be?

Dr. KUPFER. What I. as Director of the National Eye Institute. am more concerned about is the number of ophthalmologists who are conducting research rather than the ophthalmologists delivering eye care.

Mr. FLOOD. All right you are, but I am interested in how many should there be.

Dr. KUPFER. I am afraid I don't have a good answer to that question.

Mr. FLOOD. An educated guess.

Dr. KUPFER. I think the problem is that distribution of ophthalmologists and of physicians in general does represent a problem.

Mr. FLOOD. I am not going to get anyplace with that I can see. How many new ophthalmologists are licensed every year?

Dr. KUPFER. About 400 are board certified each year.

Mr. FLOOD. What is the difference between an ophthalmologist and optometrist?

Dr. KUPFER. An ophthalmologist is a physician who takes training after receiving his medical degree for the surgical and medical treatment of eye diseases. An optometrist is a professional who attends a school of optometry and is licensed for the diagnosis and treatment of refractive disorders of the eye and for the detection and treatment of certain other eye conditions.

Mr. FLOOD. He is not merely a paramedic?

Dr. KUPFER. No, sir.

Mr. FLOOD. How many optometrists are there in the United States?

Dr. KUPFER. Approximately 18,600 who are actively practicing optometry. There are an additional 2,000 or so who are licensed but not actively practicing.

Mr. FLOOD. This research you have been talking about, is any of that conducted by optometrists?

Dr. KUPFER. Yes, sir, definitely.

INTRAMURAL RESEARCH PROGRAM

Mr. FLOOD. Tell us about a few of the projects that you are carrying on through your intramural research program.

Dr. KUPFER. I have mentioned the very strong cataract research group, and I mentioned last year the work of Dr. Kinoshita in the sugar cataracts. That work is ongoing. From a clinical point of view, we are much interested in a new operative procedure——

Mr. FLOOD. At that point or at some point you might bring us up to date on that research Dr. Kinoshita is doing.

Dr. KUPFER. Yes, sir.

Perhaps I could do that right now.

Last year I reported on Dr. Kinoshita's research in which the lens placed in a test tube and given too much sugar became opaque, in other words a cataract developed, Dr. Kinoshita was able to delay this cataract from developing in the test tube by using a drug which protected the lens. This year he has been able to repeat these experiments in living animals, and not only has he been able to delay the cataract from forming by giving the drug by mouth, but he has now been able to delay the cataract from forming by giving the drug in the form of drops. So that the long-awaited idea of actually influencing the development of a cataract by eye drops is a possibility now in that limited situation.

Mr. FLOOD. Suppose you go on on your intramural program.

DIABETIC RETINOPATHY

Dr. KUPFER. In the clinical program that we have intramurally, we are very interested in a technique that promises to be of great value to many patients with retinal disease, especially those with diabetic retinopathy. I think you are aware of how much more important diabetes has become in contributing to blindness in patients who have had diabetes a number of years. Twenty years ago it was unusual to have a patient with diabetes who had any problem with his vision, but today it is the second main cause for new adult blindness and very rapidly appears to be on its way to be the main cause of new adult blindness.

One of the ways that diabetes causes blindness is that——

Mr. FLOOD. You mean you just found that out, or is it a condition that happened all of a sudden?

Dr. KUPFER. No, sir. The eye complications from diabetes are related to the length of time the individual has diabetes. As you know, the average lifespan of the diabetic had always been very short until the advent of insulin which took place back in the 1920's. So we are now beginning to see individuals who are living fuller, longer lives, and they are beginning to develop these complications which we did not see 20 years ago because the diabetes interfered with their length of life.

The way that diabetes causes loss of vision is that new fragile vessels develop in the retina and bleed into the vitreous. I think you have before you a photograph of the diagram of the eye showing the large space in front of the retina and behind the lens. That is called the vitreous. If that fills up with blood, it is apparent light can't reach the retina, the seeing part of the eye.

With the support of National Eye Institute funds, a new technique has been developed to remove that diseased vitreous and with it, of course, the blood or any other scar tissue that would form. This operation is called vitrectomy, and it has given vision to patients who, for 1, 2, or 3 years, have not been able to see anything more than light or darkness. So it has been a very dramatic change in the treatment of individuals.

INTRAMURAL RESEARCH

Mr. FLOOD. I wish you would develop for the record more testimony with reference to your intramural program.

Dr. KUPFER. Yes, sir.

[The information follows:]

INTRAMURAL RESEARCH PROGRAM

The National Eye Institute's intramural research program, the smallest of those of the National Institutes of Health, consists of laboratory and clinical research on leading causes of blindness and visual disability in the United States.

In the laboratory of vision research, animal models for two retinal dystrophies that occur in humans are being actively investigated. One of these, retinitis pigmentosa, is an inherited disorder leading to night blindness and gradual loss of visual function.

Research is underway directed toward improved understanding of the mechanisms which control development of the eye. This study is shedding light on the cause of many congenital eye defects. The pathological changes that occur in the cells of the eye that produce aqueous when the intraocular pressure is higher or lower than normal are also being examined. These studies are needed to better understand the nature of glaucoma.

In addition to these clinically related studies, as well as the cataract research referred to elsewhere in this testimony, more basic problems are being approached with the aim of understanding better how the eye functions and establishing the basis for unraveling the sequence of events that occurs in various disease processes.

The Clinical Branch of the intramural programs of the National Eye Institute has research underway on diabetic retinopathy, glaucoma, and retinal degenerations.

The facilities for these investigations are located in the Clinical Center of the National Institutes of Health and consist of 26 hospital beds assigned to investigation of eye diseases, and outpatient department, and laboratory facilities. The Clinical Branch furnishes ophthalmologic consulation to the clinical research programs of the other Institutes, and through these contacts has almost unique opportunities to investigate a series of patients with rare metabolic diseases that have been thoroughly examined by the other Institutes.

An example of this kind of cooperation is in our study of the relationship of growth hormone to diabetic retinopathy. In the National Institute of Arthritis, Metabolism, and Digestive Diseases, a large number of patients with acromegaly have been under study for many years. There is some indication that these patients occasionally have retinal blood vessel disease similar to that of diabetic retinopathy. There is reason to believe that this condition is caused by the excess of growth hormone which these patients have. The Eye Institute has been able to study the blood vessel changes in these patients and correlate them with other features which have already been recorded.

From this study, we may get a clue as to the role of the growth hormone in contributing to diabetic retinopathy.

The treatment of diabetic retinopathy with laser photocoagulation results in some unavoidable injury to the retina. The extent of this injury is being studied and correlated with the methods of treatment.

Additionally, in the advanced stages of diabetic retinopathy, there is a growth of new blood vessels into the vitreous cavity and on the retina. These growths eventually destroy the vision by producing detachments of the retina. The vitrectomy operation has been developed to palliate the vitreous disease. In the Clinical Branch, the diseased vitreous removed at operation is being tested to see if a factor can be isolated from it which stimulates the growth of new blood vessels. If such a factor can be isolated, the conditions under which it is produced can be studied, and it may be possible either to control the production of this factor or protect the eye against its effect.

Studies are also underway to determine which measurements that could be made in detecting glaucoma are most likely to indicate which patients are in danger of losing visual function from this disorder. The effectiveness of early treatment of elevated intraocular pressure in preventing injury to vision is being studied. Another series of investigations in normal volunteers is describing more precisely what factors control the intraocular pressure and how these are controlled by drugs.

In another aspect of the glaucoma problem, the development of methods to grow the diseased eye tissue which causes obstruction to fluid outflow from the eye—the trabecular meshwork—in tissue culture is underway. It is hoped that a study of the tissues responsible for the obstruction of the drainage of aqueous humor in glaucoma may give clues to the underlying cause and eventual prevention of the chronic form of this disease.

Other projects at the Clinical Center are the development of tissue culture methods for the study of retinitis pigmentosa and other retinal degenerative disease, the establishment of a clinic for the study of ocular birth defects and ocular disease of the neonatal period, the trial of a method for detecting one form of eye cancer (malignant melanoma) using a radiolabeled drug which concentrates in tumors, and a study of the immunologic factors involved in rejection of corneal transplantation.

Mr. Flood. Your budget shows 73 jobs there for intramural laboratory and clinical research. Can you give us a breakdown of those positions by the type of project and give us an idea of how many people are working on each project?

Dr. Kupfer. Yes, sir.

[The information follows:]

ASSIGNMENT OF INTRAMURAL RESEARCH INVESTIGATORS[1]

	Current professional staff			Estimated percent of existing blindness
	LVR	CB	Total	
Retinal and choroidal diseases	9	4	13	39
Cataract	4	0	4	15
Glaucoma	1	3	4	13
Corneal diseases	0	0	0	6
Sensory motor disorders and rehabilitation	3	0	3	27
Research support staff	17	7	24	100
Other: Administrative, clerical, technical, research support, and clinical associates			49	
Total, intramural	17	7	73	100

[1] This analysis reflects the many areas of research activity being carried out in the NEI intramural research program including those where there is little coverage or no activity at all.

NIH SALARY RESTRICTIONS

Mr. FLOOD. Do you find salary restrictions making it difficult to recruit and retain research personnel?

Dr. KUPFER. Sir, I am glad you asked the question in terms of recruit and retain. I think if one is recruiting young individuals, we are competitive with academic institutions. But very quickly after several years such a young individual, especially if he is good—and if we recruit him he usually is good and promising—very quickly he finds that the differential between what is available in the academic institution and what is available at the National Institutes of Health is quite large, and the retention of such an individual is a problem.

TRACHOMA

Mr. FLOOD. I understand that the corneal diseases, especially trachoma, are the main causes of blindness throughout the world, but that these diseases are of relative insignificance here in the United States. Is that right?

Dr. KUPFER. Yes; trachoma is the main cause of blindness throughout the world and it is a minor contribution to blindness in the United States.

Mr. FLOOD. I understand trachoma is a severe health problem for the rural poor and the American Indian.

Dr. KUPFER. Yes.

Mr. FLOOD. Why is that?

Dr. KUPFER. I think one of the problems is that trachoma does become a problem where the level of distribution of water and public sanitation is not of a very high quality, and I think this is probably a main contributing factor not only in this country but all over the world.

Mr. FLOOD. What causes trachoma?

Dr. KUPFER. Trachoma is caused by an organism which is a little larger than a virus but a little smaller than a bacteria. It is sort of in between and it is transmitted by direct contact. But it can be well controlled by a high level of public sanitation and hygiene.

Mr. FLOOD. Is there a cure for trachoma?

Dr. Kupfer. Yes, sir, there is a cure. It does respond to antibiotics but the problem is one can cure it and then have a reinfection very soon after.

CORNEAL TRANSPLANTATION

Mr. Flood. You mentioned your efforts to improve the success rate in corneal transplants.

Dr. Kupfer. Yes, sir.

Mr. Flood. Since you use the term "success rate," what is the present success rate?

Dr. Kupfer. At present corneal transplantation is probably the most successful transplantation. In certain types of corneal disease it is successful 85 to 90 percent of the time. We are now looking at that remaining 10 or 15 percent, as well as cases where the success rate is lower, and we would like to raise that percentage. These, of course, are the most difficult cases.

MECHANICAL SEEING AID

Mr. Flood. We always use the term "hardware" sooner or later in your shop. Last year you mentioned a device which was being used at various schools for the blind which would help the blind people to "see."

How is that working out?

Dr. Kupfer. This is a project we have supported for a number of years. The translation of light into touch and by having a pattern of stimuli on an individual's back or abdomen the feel of what he "sees" can be translated into actual visual images.

This research is continuing and is being tested at a number of schools for the blind around the country. I think it is going to be another 2 or 3 years before we have definite information on how successful this is.

Mr. Flood. On page 116 of your justifications, and I quote, is this "the lightweight portable seeing aid?"

Dr. Kupfer. Yes, sir. At the moment it is not portable but this is being worked on.

GLAUCOMA

Mr. Flood. What causes glaucoma?

Dr. Kupfer. Ordinarily fluid is continually produced in the eye to nourish the tissues inside the eye and continually draining off. If the drainage becomes clogged, the fluid is produced and pressure begins to rise.

Mr. Flood. Can you cure it?

Dr. Kupfer. There are some types of glaucoma we can cure. Congenital glaucoma occurring in infants if caught early enough, can be cured. Acute glaucoma accompanied by severe pain and redness of the eyes, if caught early enough can be completely cured.

The usual glaucoma, the so-called open-angle glaucoma or chronic glaucoma can't be cured. It can be controlled, however, with medicine and, where necessary, surgery.

Mr. Flood. Is there an increase in the incidence of glaucoma?

Dr. Kupfer. Not to our knowledge, sir.

Mr. Flood. Are there any research leads, anything at all, red hot, which cannot be pursued because of lack of funds?

Dr. Kupfer. I would say in general if we have a red hot research lead we then make this our top priority and there is a movement of resources to support that type of activity.

RETINAL DISEASES

Mr. Flood. You mention the retinal diseases are responsible for more blindness and visual disability than any other cause. Is it primarily older people who are affected by these diseases?

Dr. Kupfer. Yes, to a great extent, but retinal degenerations can occur in childhood and in young adulthood as well as in older age groups.

Mr. Flood. Again I am going to quote from the justifications. "Major emphasis will be placed on increasing the base scientific information required for an all out clinical attack against several diseases of the retina."

When do you expect it will be possible to "mount this all out attack or charge"?

Dr. Kupfer. In the case of diseases such as glaucoma we do have a rather substantial research base upon which we are mounting direct clinical programs. But in the case of retinal disease we have a tremendous amount of basic information that must be learned about the retina before we can mount this clinical attack. I don't know how long it is going to take, but I think we have got to get on with the job as soon as possible.

TRAINING PROGRAMS

Mr. Flood. Doctor, here we go again. Your budget here looks pretty much like all of the other Institutes, a standstill budget for research and phasing out training grants. Do you think phasing out training grants is wise? Do you think the training programs in this field are going to go on after all of this Federal support is withdrawn from them?

Dr. Kupfer. I think what we are hoping, Congressman, is that the fellowship program will maintain the level of training activities. We do have a rather unique problem with training, and that is we do not offer research training to the ophthalmologist until he has completed his clinical training. This means he has been through medical school and a year of internship and 3 years of advanced postgraduate training——

Mr. Flood. You just said 12 years didn't you?

Dr. Kupfer. That is right. And then we ask him to learn the approaches of research. At this rather advanced stage, it would be very desirable to be able to have a much broader based program, but we have our hopes on the fellowship program at the present time.

Mr. Flood. For the record, we want information as to the 1973 funds obligated in 1974 and the multiple-year funding of grants and contracts, the same kind of thing we requested from all of the other Institutes.

Dr. Kupfer. Yes, sir.

[The information follows:]

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
NATIONAL INSTITUTES OF HEALTH
National Eye Institute

Obligations by Budget Mechanism
Showing "True" Program Levels
in 1974 - 1975
(Amounts in thousands)

Budget Mechanism	1972		1973		1974		1975	
	No.	Amount	No.	Amount	No.	Amount	No.	Amount
GRANTS:								
Regular								
Non-competing	291	16,486	287	16,532	276	17,134	326	20,831
Competing	53	3,395	45	2,801	60	3,766	41	2,957
New	77	3,278	73	2,952	51	4,279	66	3,883
Supplemental	(9)	189	(10)	145	(5)	81	(4)	50
Subtotal	421	23,348	405	22,430	387	25,260	433	27,721
Special								
Research Career Program	16	379	17	512	17	529	19	529
Scientific Evaluation	---	25	---	15	---	60	---	70
Subtotal	16	404	17	527	17	589	19	599
TOTAL, GRANTS	437	23,752	422	22,957	404	25,849	452	28,320
Fellowships								
Non-competing	1	15	40	428	30	403	123	1,882
Competing	10	85	---	5	---	---	---	---
New	96	1,197	17	290	116	1,784	53	771
Supplemental	---	---	---	---	---	---	---	---
Subtotal	107	1,297	57	723	146	2,187	176	2,653
Training Grants								
Non-competing	31	2,174	37	2,101	41	3,449	30	1,994
Competing	10	573	6	343	---	---	---	---
New	5	251	---	---	8	408	---	---
Supplemental	---	---	---	---	---	---	---	---
Subtotal	46	2,998	43	2,444	49	3,857	30	1,994

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
NATIONAL INSTITUTES OF HEALTH
National Eye Institute

Obligations by Budget Mechanism
Showing "True" Program Levels
in 1974 - 1975
(Amounts in thousands)

Budget Mechanism	1972		1973		1974		1975	
	No.	Amount	No.	Amount	No.	Amount	No.	Amount
Laboratory and Clinical Research.....	68	3,376	71	3,583	73	4,323	73	4,458
Research and Development Contracts...	---	2,262	---	2,122	---	2,122	---	2,322
Biometry, Epidemiology and Field Studies......................	---	311	---	420	---	475	---	487
Research Management and Program Services.........................	70	1,347	63	1,653	55	1,919	55	1,974
Total..............................	138	35,343	134	33,902	128	40,732	128	42,208

Obligations by Budget Activity
Showing "True" Program Levels
in 1974 - 1975

(Amounts in thousands)

Budget Program	1973		1974		1975	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Retinal and Choroidal diseases	---	$11,565	---	$12,678	---	$13,325
Corneal diseases	---	4,828	---	6,174	---	6,469
Cataract	---	2,388	---	3,077	---	3,213
Glaucoma	---	3,542	---	4,580	---	4,767
Sensory-motor Disorders & Rehabilitation	---	6,343	---	7,506	---	8,002
Intramural Laboratory & Clinical Research	71	3,583	73	4,323	73	4,458
Research Management & Program Services	63	1,653	55	2,394	55	1,974
Total, NEI	134	$33,902	128	$40,732	128	$42,208

NATIONAL EYE INSTITUTE

Distribution of 1973
Impounded Funds
(Amounts in thousands)

Budget Mechanism	No. of Awards	Amount	Remarks
Research Grants	9	528	Retinal & Choroidal Diseases
	6	277	Corneal Diseases
	2	151	Cataract
	3	181	Glaucoma
	7	359	Sensory Motor Disorders & Rehabilitation
Fellowships	6	92	Retinal & Choroidal Diseases
	13	201	Corneal Diseases
	5	79	Cataract
	2	30	Glaucoma
	9	133	Sensory Motor Disorders & Rehabilitation
Training Grants	3	426	Retinal & Choroidal Diseases
	1	91	Corneal Diseases
	1	157	Cataract
	2	239	Glaucoma
	1	41	Sensory Motor Disorders & Rehabilitation
Research & Development Contracts	--	---	---
Total	70	2,985	

NATIONAL EYE INSTITUTE

Multi-year Funding from 1974 Appropriation

(Amount in thousands)

Budget Mechanism	No. of Awards	Total Amount	Amount Affecting 1975 Funding	Remarks
Research Grants	23	$1,944	$972	Retinal & Choroidal Diseases
	5	406	203	Corneal Diseases
	2	138	69	Cataract
	13	1,130	565	Glaucoma
	10	904	452	Sensory Motor Disorders & Rehabilitation
Fellowships	--	---	---	---
Training Grants	--	---	---	---
Research & Development Contracts	--	---	---	---
Total	53	4,522	2,261	

Mr. **Flood**. Mr. Robinson.

Mr. **Robinson**. Thank you, Mr. Chairman.

INCIDENCE OF EYE DISORDERS

Doctor, I wonder if you could estimate or if you have a percentage figure as to the extent of the population which is seen by an eye specialist at some point in his or her lifetime?

Dr. **Kupfer**. Perhaps I could start by saying that probably about 100 million people or half of the population wear glasses. Therefore, I would say the majority of these individuals have had to see an eye specialist at some time.

In addition to that group, there are the individuals who would seek medical care because of other eye diseases.

Mr. **Robinson**. This is the group I had reference to, not those that might perhaps go no further than consulting an oculist but those that do see an ophthalmologist.

Dr. **Kupfer**. Yes, sir. There are statistics to show that the number of patients visiting ophthalmologists is approximately 1 million per week.

Also, if you look at the patients coming to a general hospital, about 15 percent go to the eye clinic. That is a substantial number.

There are more eye patients hospitalized in hospitals for surgical care than any other category.

The exact answer to your question is difficult but I certainly think that a significant number of Americans seek eye care.

Mr. **Robinson**. I understand that the majority of those that are hospitalized are hospitalized for surgery.

Dr. **Kupfer**. Yes, sir.

GLAUCOMA

Mr. **Robinson**. I happen to be one who has the beginning of glaucoma and I have to take the usual drugs for it. I don't know how to identify which one I am taking because I am not familiar with the generic name. But I am interested in your statement with regard to the cause of glaucoma in that the release of pressure within the eye is because a little duct gets closed and that the fluid continues to generate and the pressure builds up. Is it not true high blood pressure also is a factor in this matter to an extent that it is considered to be significant?

Dr. **Kupfer**. In general high blood pressure doesn't seem to contribute to the buildup of pressure in the eye. As a matter of fact, high blood pressure tends to protect the eye against some of the effects of this pressure in the eye.

Mr. **Robinson**. Just as one individual I might report that I have been sadly misinformed then because I had associated high blood pressure and the tendency toward glaucoma to an extent I thought that the two, to a degree, certainly went hand in hand, and if you had high blood pressure your internist would like to send you to the ophthalmologist to see whether or not you had the beginnings of glaucoma. But this is not medically factual?

Dr. **Kupfer**. No, sir.

Mr. **Smith**. Will the gentleman yield?

Mr. **Robinson**. Yes.

Mr. **Smith**. Does low blood pressure contribute?

Dr. Kupfer. No, sir. But again the individual who does have increased pressure in his eye is more prone to get into trouble as far as the function of his eye is concerned than if he has low blood pressure, and less involved if he has higher blood pressure.

Mr. Smith. It doesn't cause it then but it can cause trouble afterward?

Dr. Kupfer. Yes, sir.

Mr. Robinson. You mention the fact that you have found an animal model in a certain type of monkey that assists you in the research regarding glaucoma. How can you measure the angle of vision of a monkey?

Dr. Kupfer. You mean the visual field?

Mr. Robinson. Yes.

Dr. Kupfer. At the present time there is no easy way of doing this. What we depend upon is to find the changes in the back of the eye in the retina and in the optic nerve.

Mr. Robinson. It is by observation?

Dr. Kupfer. Yes, sir.

Mr. Robinson. I have heard some ophthalmologists state that the process by which the pictures are taken of the back of the eye is not necessarily good for the eye, that you should do this as seldom as possible because of the extreme dilation that is necessary. Is this generally accepted?

Dr. Kupfer. There are literally thousands of pictures taken everyday throughout the country, if not the world, of the back of the eye through dilated pupils. I am not aware of any evidence that this has been deleterious. I think there are some individuals in whom one must be very careful before one dilates the pupil, but these are identified by opthalmologists, and of course, care is taken.

CORNEAL DONOR PROGRAM

Mr. Robinson. What is your appraisal of the success and the potential of the corneal donor program?

Dr. Kupfer. There are two levels at which the success should really be measured.

The first and most immediate has been the making available of corneal donor material. I think this has really revolutionized the development of corneal surgery in the United States. I think we are pre-eminent in the world in this respect, partly because of the corneal donor program.

There is a second aspect which is in some respects as important, if not more so, and that is that there are eyes donated through eye banks which are not primarily used to supply corneal material but are used for other research purposes. I think this is a very important way to learn more about other eye diseases. So I would say it has been successful on two fronts.

Mr. Robinson. I was referring more to the extent to which it is increasing or decreasing or maintaining status quo. Just what is the status of the program in terms of participation by the general public, the advanced knowledge of the existence of it and potential donors doing the necessary paperwork in advance?

Dr. Kupfer. It is my perception that the number of eyes that are donated is increasing, but that our need for corneal donor material is still great, in part because additional material is required for eye research purposes.

EYEBANK

Mr. Robinson. Do you participate to any extent in publicizing the eyebank program in an effort to promote an understanding and participation by the general public in this program?

Dr. Kupfer. No, sir. The National Eye Institute is not primarily active in this area. We do have our own eyebank at the National Institutes of Health Clinical Center, to take care of our needs for corneal transplants and research programs, but we do not take part in the national eyebank program.

Mr. Robinson. That is all, Mr. Chairman. Thank you.

Mr. Flood. Mr. Smith.

GLAUCOMA

Mr. Smith. With regard to glaucoma, they give examinations looking into the eye. Are there methods of early detection?

Dr. Kupfer. We are supporting some research in the area of early detection. As I mentioned last year, this is one of the areas that we feel should receive some increased research emphasis, because if we feel we can control the glaucoma once it is detected, it becomes very important to detect it early.

We are at present trying to improve methods of examining the back of the eye, perhaps by just taking a photograph and then reading all of these photographs to determine which individuals seem to be at high risk. And perhaps by next year we will have the preliminary answers to these approaches.

Mr. Smith. You mentioned red eyes and so forth. I am not quite sure what that has to do with glaucoma.

Dr. Kupfer. I am sorry.

Mr. Smith. You mentioned earlier red eyes and bloodshot and so forth. What does that have to do with glaucoma?

Dr. Kupfer. I see. There is one type of glaucoma in which the individual develops very severe pains in and about his eye, as well as a very red eye. The pressure rises very rapidly, usually within an hour or 2. This is called acute glaucoma because it occurs suddenly. We can now cure this condition if it is caught early at the acute stage.

Mr. Smith. You mean he gets it and then gets over it?

Dr. Kupfer. The individual may have an attack of acute glaucoma, and either it spontaneously clears, which doesn't frequently happen, or the pressure remains elevated for 2 or 3 days and destroys most of the eyesight, or he is seen by an ophthalmologist fairly early, and an operation is done which completely cures the eye of ever having another attack.

Mr. Smith. Then this is something that causes permanent damage?

Dr. Kupfer. Yes, sir; if left untreated, it definitely does.

Mr. Smith. Since that is the principal eye disease, is enough research being done on glaucoma?

Dr. Kupfer. I think the deployment of resources has been in the areas where the needs are greatest, such as in early diagnosis. But of course, whenever one moves resources from one program to another, this leaves less priority items uncovered.

Mr. Smith. If there were more money, are there more things that could be done?

Dr. KUPFER. Yes, sir.

Mr. SMITH. That is all I have.

Mr. FLOOD. Mr. Patten.

Mr. PATTEN. Thank you, Mr. Chairman.

We are going to go along with about $3 million less than last year, as I read the totals. It is $42 million, and you will have a $3 million decrease despite the inflation and everything else.

When asked to start a conversation about man's worst affliction, I suggested blindness. I suppose nobody would find much fault with that, would they?

Dr. KUPFER. No, sir.

Mr. PATTEN. Even though that wouldn't be the end of the conversation. But you could readily put blindness up there as No. 1.

You didn't say much about preventive measures. You have used the connection one or two times. But I have heard eye people claim we have a lot better job to do in preventive work. If every ophthalmologist around the country would look for cancer or would look for signs of hardening and other things, take a little time, a great deal of good work could be done. I suppose we have to rely upon the professionals to do that.

I don't know how many people never see an eye doctor. I guess there are many areas around the country without eye doctors.

Dr. KUPFER. Yes, sir.

Mr. PATTEN. Senior citizens that want a pair of glasses are paying $72. I don't think this is right, particularly when you have $140 a month to live on. The result is they won't go to the eye doctor.

With some Federal money, we take our older people by bus to a county hospital for a free examination, and the program is very popular. The results of this work are well worthwhile. I know these older people feel they cannot go to a doctor or dentist or eye doctor. They hesitate. You really have to push them.

CANCER OF THE EYE

You didn't say much about cancer of the eye. Is that much of a factor?

Dr. KUPFER. I am glad you mentioned that. Although cancer of the eye isn't a main cause of blindness, it is the one disease which results in death. We usually deal with individuals who do not die from their eye disease, but of course they are either rendered blind or with a very severe visual handicap.

We are concerned about cancer of the eye. As a matter of fact in our intramural program, and I will provide this for the record, we have a very active group looking at better ways of diagnosing cancer in the back of the eye. So this does account for some of our activities in Bethesda.

The newer techniques that are being developed in the treatment of cancer elsewhere in the body are being applied now to the cancers of the eye.

Mr. PATTEN. I heard a cancer doctor say very strongly that this should have been seen earlier. It shouldn't have been left so long. He spoke as if it was inexcusable that a particular patient with cancer of the eye should have reached him at such a late stage. He was distressed by it, especially since the patient had been to an opthalmologist and nobody saw it.

I think he said it could have been seen months before coming on.

You said the cataract surgery is painless.

Dr. KUPFER. Yes, sir.

Mr. PATTEN. You didn't mean financially.

EFFECTS OF SMOKING

You didn't say anything about the effect of smoking on the eye. Is this part of your work? It strikes me when you smoke a cigarette there must be some ammonia in that smoke and there might even be a little carbon monoxide, right?

Dr. KUPFER. Yes, sir.

Mr. PATTEN. There must be a lot of things in that smoke that don't do the eyes good. Is there any validity in my statement?

Dr. KUPFER. Yes, sir. We do support some research on the effect not only of smoke but of other environmental factors on the eye. Individuals who do have eyes that are particularly prone to local irritation, their eyes become red when they go into a smoke filled room.

Mr. PATTEN. Were you ever in Los Angeles?

Dr. KUPFER. Yes, sir. That is where the research is ongoing.

Mr. PATTEN. I know if you get into a room and the crowd are all smoking it is unbearable. We have this little fight about should you be allowed to smoke on an airplane, should you allow the last four seats to be for smokers or have a special car for smokers.

It would seem to me that smoking, especially where everybody is smoking in a crowded room and you are not getting ventilation must affect the eyes. I think that is common knowledge. Right?

Dr. KUPFER. Yes, sir.

Mr. PATTEN. I am sitting here listening to requests for $100 million more for cancer and it strikes me I can be a good advocate for your department, and most of all, for providing funds to enable some smart young people to work on things you mentioned. I don't need any more testimony on whether or not I will vote for grant money or fellowships for your department. I take for granted we can accomplish a great deal.

FOREIGN CONTRIBUTIONS TO EYE RESEARCH

I have one other thought. We had the Russians in here yesterday. What contribution do other countries make in your accumulation of knowledge? Do the French or English or Germans, Japanese and other people make a contribution of work similar to yours?

Dr. KUPFER. Yes, sir. There is active eye research in all of the countries you mentioned.

As far as the Soviet Union is concerned, they have recently presented a new treatment for glaucoma in which they use a very special laser, not the usual type of laser, but a very special laser to make a small opening in the outflow channel that becomes closed up. We at the intramural research program in Bethesda are in the process of building one of these instruments to first test it out on experimental animals to see if in fact it does have value. So you are right; there are contributions from other countries and we are in close touch with them in following up any promising leads.

Mr. PATTEN. Thank you, Mr. Chairman.

EYE TESTS FOR THE ILLITERATE

Mr. SMITH. How do you give eye tests to people who are illiterate or can't read?

Dr. KUPFER. There is a special eye chart for this purpose which consists of the letter E with the bars pointing either down or up or sideways, and we just have the individual hold his fingers in the appropriate direction.

Mr. SMITH. Line on the eye charts?

Dr. KUPFER. Yes, sir.

Mr. FLOOD. Mr. Robinson.

DIABETES

Mr. ROBINSON. We hear a great deal about diabetes today and I haven't heard you mention, doctor, to what extent diabetes contributes to the eye problems which you have to concern yourself with today?

Dr. KUPFER. Diabetes is getting to be more and more of a cause of blindness in the American population. This is related to the fact that the diabetes causing blindness is not related to the severity of diabetes but how long the patient has had diabetes. So that as more and more people live longer and longer with diabetes we are beginning to see the eye complication. At the present time diabetic retinopathy, which is the name given to the effect of diabetes on the retina, is the second main cause of new adult blindness and is very rapidly moving into the first spot.

We are very, very concerned about this problem. We are supporting a very extensive program in testing a certain type of treatment in diabetics. This represents a very significant amount of our resources, and we are doing a national cooperative study among 16 medical centers to test this treatment.

In addition, I think a lot of our information about the way diabetes affects the retina will come from basic research we are supporting. About $12 million of our entire budget is in retinal research.

Finally we are in our intramural laboratories using a technique called vitrectomy in which the ravages of diabetic retinopathy, the bleeding of the vessels into the back of the eye, can be reversed. So far this has been very exciting, very promising, and we are pursuing it very aggressively. We are aware of the importance of diabetes, and we are very active in pursuing whatever leads are available.

RESEARCH PRIORITIES

Mr. ROBINSON. Finally, doctor, do you think that the distribution of the funds which you request with regard to fiscal year 1975 generally reflects the proper priorities that exist in eye problems today?

Dr. KUPFER. Yes, sir, in the sense that, if we look at the percentage of our resources going to retinal disease or cataract or glaucoma and the percent of blindness or visual disability that these particular diseases contribute, they match rather closely.

Mr. ROBINSON. Thank you very much.

Mr. PATTEN. Are there any blind people on your staff? Have you any use for them on computers?

Dr. KUPFER. There are a number of blind people who do transcribing and also who do computer programing at the National Institutes of Health.

EXTENT OF EYE DISEASE AND PREVENTION

Mr. Michel. Dr. Kupfer, you speak of the great progress which research has made possible in eye care during the last two decades, and point out that generally, this has been in the area of treatment and cure. Then, you underline the need for research in the area of prevention. Let me ask you first, do we have any accurate statistics that would show whether or not the actual percentage of our population suffering from diseases of the eye has diminished over the years? Then, I would like to know, does your budget lend itself to a breakdown along the "treatment-prevention" lines? That is primarily directed toward treatment and cure, from what is spent for research directed toward prevention? In what way does your new budget emphasize prevention?

Dr. Kupfer. Our statistics show that the rate of blindness in the United States has remained fairly stable in recent years. However, with the population increasing, this would indicate that the actual number of blind people is also rising. Moreover, although we have no precise statistics at the present time to indicate whether the prevalence of eye diseases has either increased or decreased, we know that as the number of aged increases, there is a subsequent increase in the number of people with eye disease. Approximately $27 million of our budget is spent on research directed toward prevention and the balance of $13 million is expended on research directed toward treatment. As you can see, the fiscal year 1975 budget places a great deal of emphasis on preventive research in that funds expended for prevention are more than twice as great as those expended for treatment.

CATARACTS

Mr. Michel. You say that "Cataract surgery, once difficult, risky, and uncomfortable to the patient, has evolved into one of the safest, most successful, and least painful of any major surgical procedure." Are you referring just to the conventional surgical procedure, or do you mean to include the use of the emulsifier instrument? The Methodist Hospital back home just put one of these instruments into use, and there has, of course, been much interest in it. What can you tell us, for the record, about the application of an instrument like this?

Dr. Kupfer. I was referring to conventional methods of cataract surgery. It is still too early to assess fully the success rate of phacoemulsification, but as the use of this technique expands, there will no doubt be studies comparing its effectiveness with conventional surgical methods. At the present time, phacoemulsification seems to be most suitable for relatively younger patients in whom the cataract has not yet hardened to the degree found in elderly patients, and for those patients who have a particular need to spend a minimal amount of time in the hospital.

Mr. Michel. Would this instrument be appropriate for use in a case where an older person has a cataract that is just beginning to blur his vision, but the doctor feels that surgery is inadvisable because of iris deterioration? What could be done in a case like that?

Dr. Kupfer. It is very difficult to comment without knowing the specific details of the case. However, I might say that generally we do not yet have enough experience with phacoemulsification to know whether it would offer any advantage in a patient with iris degeneration.

TRANSPLANTS

Mr. MICHEL. Dr. Kupfer, are you actively engaged in research relating to transplants and artificial eyes? To what extent? What long-term potential is there for either approach? You mention the development of an experimental treatment for donor corneas to inhibit their rejection as corneal transplants. What does this involve?

Dr. KUPFER. We are actively engaged in supporting research on transplantation of the cornea for use in treating certain corneal diseases. At the present time, the cornea is the only part of the eye which can be successfully grafted. Currently, the Institute is spending over $320,000 for research directly concerned with corneal transplantation. In addition, nearly $1 million is being spent on studies of the immunology of the cornea, much of which has a direct bearing on improving the outcome of corneal transplantation. Although this is one of the most successful tissue graft procedures, our aim is to extend its use to cases of corneal blindness which are currently either not amenable to this type of treatment or for which the success rate is relatively low. Examples would be damage to the cornea from chemicals and those conditions in which blood vessels infiltrate the cornea.

SIGHT SUBSTITUTION SYSTEM

To answer the second part of your question, the Institute is supporting what we believe to be the most feasible approach at this time to a sight substitution system which involves mechanical stimulation of the skin. It involves a grid pattern which, with training, a blind person can translate into images perceived as if they were in visual space. This has been likened to a more complex form of "skin writing" such as children often play, writing a word in the palm of the hand or on the back. In this case, the input for the system is provided through a television camera. The image it picks up is then broken down through a computer system into a simple outline pattern which is converted into mechanical stimulation to the skin of the abdomen. We feel this device, called the tactile visual substitution system, has enormous potential, although a considerable amount of additional research and testing will be required before it becomes a practical aid for the blind and visually handicapped.

DONOR CORNEAS

With regard to the experimental treatment for donor corneas, this is directed to the 10 to 50 percent of corneal transplants that may fail because of an immune reaction. Grantees of the Eye Institute have demonstrated in animals that it is possible to treat antibodies against this graft tissue chemically so that they will bond to the graft but not damage the transplant. It is believed that this treatment may significantly increase the chance that the graft will remain clear and reduce or eliminate the need for immuno-suppressive drugs.

Mr. MICHEL. If an individual wants to donate his corneas, how does he go about it? Who does he contact, and what is involved?

Dr. KUPFER. A person wishing to donate his or her eyes for use in corneal transplantation or for research should contact a local eye bank. These are usually listed in the telephone book. In many cases, these eye banks are supported by Lions Clubs and are affiliated with local hospitals or medical schools. In recent years, the passage of the Uniform Anatomical Gift Act, which has been adopted by almost every State, has greatly facilitated the donation of eyes and other organs for use after death. The individual simply signs a pledge card which is kept on file at the designated agency to receive the tissue and carries information concerning the pledge in case of accidential death. This procedure usually enables the removal of tissue or organs soon after death, thus assuring their viability and usefulness.

FEDERAL FUNDS FOR BLIND

Mr. CONTE. Can you give comparative figures for the annual Federal expenditure for aid to the blind as opposed to the National Eye Institute's requested annual budget?

Dr. KUPFER. The cost of blindness to public welfare agencies is approximately $468,567,000 annually. Of this the Federal Government spends $267,724,000; State governments spend $131,254,000; and private agencies spend $69,589,000.

In comparison, the National Eye Institute's budget request for fiscal year 1975 for the support of research on blinding and disabling visual disorders is $39,947,000.

CATARACT WORKSHOP

Mr. CONTE. Did the conference on cataracts last October make any budget recommendations? What did it identify as major research needs? Put that in the record.

[The information follows:]

In its final report the National Eye Institute sponsored cataract workshop identified the lack of a sufficient number of basic science and clinical investigators as the major deterrent to cataract research at the present time. They suggested that the number of principal investigators in cataract research, presently about 40, should be increased to at least 80 to 120. This represents a doubling or even tripling of the present number. To achieve this, the workshop recommended that lens research centers be established to train new investigators and to develop comprehensive research centers.

They specifically recommended that sufficient funds be provided "to train talented ophthalmologists and basic scientists at the research centers where they can obtain a well-balanced orientation in the physiology and chemistry of the normal and cataractous lens as well as orientation in clinical aspects of the disease." The group further pointed out that the training funds (training grants and career development awards) provided in the 1960's were largely responsible for the success in developing lens research during that period.

The workshop participants also agreed that "the funding of a greater proportion of research grant applications would * * * accelerate cataract research." They noted that "based on the present level of funding, support for additional grants would increase the number of ongoing programs without appreciably diminishing the quality of the research effort. At present," they said, "there are more good ideas than available money for their support."

These measures, they determined, are necessary in order to develop the following areas of promising research:

1. The elucidation of the biology and chemistry of the normal human lens which is necessary to understanding what goes wrong when cataract forms.
2. Development of better animal models for the study of human cataract. Artificially induced cataract models require more study. Furthermore, there is no

satisfactory animal model in which aging occurs with sufficient rapidity to allow careful study of the relationship of aging and cataract formation. The development of such model systems may be of fundamental importance in furthering our understanding of human cataract.

3. The intensive study of all animal models available for the purpose of establishing hypotheses to explain cataract formation at the molecular level.

4. The elucidation of the effect of factors generated outside the lens upon the development of cataract. Recent studies suggest that the retina and the vitreous may influence the development and physiology of the normal lens. The relationship of factors derived from such sources to the onset and development of cataract is not presently understood. The effect of disease ostensibly manifested in other parts of the organism should also be considered. Attention must also be given to the cooperative effect of two or more factors, no one of which is effective alone in causing cataract.

5. The definition and classification of different types of cataract and the establishment of guidelines for the recognition of different kinds of cataract development.

RESOURCE DISTRIBUTION

Mr. Conte. On page 118 of the justification, there is a reference to six Institute objectives used as the basis for all planning and evaluation activities. What are they? Were they set by the Advisory Council?

Dr. Kupfer. In order to achieve appropriate distribution of resources, the National Eye Institute is following these six objectives:

1. Stress research that is most relevant to the NEI mission.
2. Emphasize research on the most common causes of blindess and visual disability.
3. Concentrate on prevention rather than rehabilitation.
4. Categorize all NEI supported projects in terms of their bearing on etiology, diagnosis, and treatment to determine balance within a program area and to judge whether there is a sufficient scientific base on which to build an applied program to improve clinical diagnosis and therapy.
5. When the choice of animal model would not interfere with the validity of objectives of a research proposal, favor research in those forms closest to man.
6. Use whichever funding mechanism is most appropriate for the purpose being served. In general, this will mean reliance on the research grant.

These six objectives were submitted to and approved by the National Advisory Eye Council.

DIABETES EXPERTS ON ADVISORY COUNCIL

Mr. Conte. Is there a member of your advisory council who has specific interest or competence in diabetes-related visual disorders?

Dr. Kupfer. Three members of the National Advisory Eye Council are expert in retinal disease. They are Drs. Frank W. Newell, professor and chairman of the Department of Ophthalmology, Pritzker School of Medicine, University of Chicago; Charles L. Schepens, president, Retina Foundation, Boston, and Bradley R. Straatsma, director, Jules Stein Eye Institute, University of California at Los Angeles School of Medicine. These three are recognized international authorities in retinal research, including diabetic retinopathy and other diabetes-related visual disorders.

BLINDNESS IN CHILDREN

Mr. CONTE. What are the causes of severe vision problems, and blindness, in children?

Dr. KUPFER. According to a study conducted by the National Eye Institute, there are at least 32,000 blind persons under age 20. Major causes of such blindness are congenital and developmental defects of the visual system including cataract, retinal diseases, and optic nerve atrophy. In children under 5 years of age, retinal diseases as a group account for about 20 percent of all blindness; in the age group 5 to 19, retinal diseases are responsible for about 23 percent of all blindness. Overall, prenatal influences including cataract and retinal degeneration are responsible for the greatest amount of juvenile blindness.

CORNEAL TRANSPLANTS

Mr. CONTE. What is the ratio of available corneal transplants to those needing them?

Dr. KUPFER. The exact ratio of available eyes for corneal transplantation to the number of transplants actually needed is not known. This is because there have been no definitive studies conducted by any governmental or private organization in this area. However, it is generally agreed that the number of corneas needed for transplantation far exceeds the number of tissues which are available. For example, in the Washington, D.C. area approximately 72 eyes are collected each month. When fresh tissue becomes available, the donor cornea is usually used immediately if it is suitable for transplantation to a recipient. Despite the number of corneas which do become available each month, there are between 45 to 50 patients in the Washington area who are now on waiting lists for corneal transplantation when suitable tissue becomes available. Corneas which cannot be used immediately are either preserved through a technique called cryopreservation which employs extreme cold or are dehydrated and sent to another area of the country where they are needed at once.

Last year the Washington Eye Bank & Research Foundation collected 648 eyes and was able to use 285 for transplantation. The remainder were preserved or sent elsewhere where they were needed. It is important to note that even though more eyes were collected than could be used, this is the result of donor corneas not meeting the specific requirements of the tissue needed for transplantation and does not reflect a surplus of available tissue.

GLAUCOMA

Mr. CONTE. Has the new drug for treating glaucoma been released by the FDA for general use?

Dr. KUPFER. No, 6-hydroxydopamine is still considered experimental by the Food and Drug Administration and has not yet been released for general use. Generally, the FDA does not conduct its own drug investigations but rather evaluates the results of those investigators who are studying the particular drug and makes its determination based on a series of studies. In most cases a drug undergoing investigation will pass through a series of phases before it is recommended by the FDA for general use. In the case of 6-hydroxydopamine, the drug has already undergone a number of tests and is now considered to be in the investigational new drug status.

VISION RESEARCH SUBCOMMITTEE

Mr. CONTE. Is your advisory council subcommittee looking at program balance also concerned with level of support? Has it made any recommendations on level of support or on kind of support, grants versus contracts, etc.?

Dr. KUPFER. The Vision Research Program Planning Subcommittee of the National Advisory Eye Council is concerned with overall levels of support as well as program balance. In fact, one of the major functions of the subcommittee is to provide the council with advice regarding establishment of funding priorities, determination of appropriate distribution of resources, and identification of research priorities.

Thus far, the subcommittee has already pointed out some neglected research opportunities in retina which should be further expanded. This is the result of a detailed review and analysis of the retinal and choroidal diseases program which showed that, while overall distribution is good, more clinical research needs to be stimulated and additional basic laboratory work, emphasizing prevention of retinal diseases, need to be undertaken.

The subcommittee has not yet issued a final report on their findings. Four research areas still must be considered, and it is expected that recommendations as to the appropriate distribution of resources or needs for expanded programs will be made when analysis and evaluation of these four areas are completed.

One of the principles that the National Advisory Eye Council has asked the subcommittee to operate under is that the funding mechanism to be used for research support should be the one most appropriate for the purpose being served. In most cases this means that the research grant will be used.

"ARTIFICIAL EYE"

Mr. CONTE. Just this past week an article appeared in one of my local newspapers about an artificial eye which has been developed by a team of scientists and engineers at the University of Utah. It sounds amazing to me. Would you please comment on this article?

Dr. KUPFER. Development of the artificial vision system explained in the article was supported for about 2½ years by the National Institute of Neurological Diseases and Stroke, as part of their neural prostheses program. Although Dr. William Dobelle is no longer receiving support from the NINDS for his work in stimulating the visual cortex of the brain, that Institute is still supporting studies to determine the feasibility of visual as well as other neural prostheses projects.

A device developed with NEI support already being widely used is the Optacon which enables the blind to read the same printed material as any sighted person. It presents a tactile facsimile image of printed characters which are scanned by an optical probe. Instead of Braille impressions, the user of the Optacon senses the outline of a regular letter conveyed through raising and lowering of an array of tiny rods which fit onto a single finger. This system is already on the market and is being further developed for use as a mobility aid.

Mr. FLOOD. Thank you very much.

Dr. KUPFER. Thank you.

JUSTIFICATION OF THE BUDGET ESTIMATES

NATIONAL INSTITUTES OF HEALTH

National Eye Institute

Amounts Available for Obligation

	1974 Revised	1975
Appropriation	$41,631,000	$39,947,000
Amount withheld (PL 93-192)	1,684,000	---
Subtotal, adjusted appropriation	39,947,000	39,947,000
Real transfer to:		
"Departmental Management" (For Department-wide reductions in public affairs)	-9,000	---
Comparative transfer from:		
"National Institute of General Medical Sciences" (Decentralization of scientific evaluation grants program)	60,000	---
Subtotal, budget authority (base obligations)	39,998,000	39,947,000
Unobligated balance, restored	4,165,000	---
Comparative transfer of restored unobligated balance to Research Resources for General Research Support Grants	-1,170,000	---
Total, obligations	$42,993,000	$39,947,000

Summary of Changes

1974 Estimate obligations	$42,993,000
1975 Estimated obligations	39,947,000
Net change	-$ 3,046,000

	1974		Change	
	Pos.	Amount	Pos.	Amount
Increases:				
A. Built-in				
1. Within-grade salary increases	--	---	--	+$42,000
2. FTS rate increase	--	---	--	+ 5,000
3. Extra day of pay	--	---	--	+ 9,000
4. Increased cost of service and supply	--	---	--	+ 3,000
5. Bureau of employees Compensation	--	---	--	+ 2,000
6. Payment to NIH Management Fund	--	---	--	+141,000
Subtotal	--	---	--	+202,000
B. Program:				
1. Research grants				
a. Noncompeting continuations	--	---	--	+$7,486,000
b. Competing (new continuations and supplementals)	--	---	--	+ 6,890,000
2. Fellowships:				
a. Noncompeting continuations	--	---	--	+ 1,784,000
b. Competing (new continuations and supplementals)	--	---	--	+ 771,000
3. Training grants:				
a. Noncompeting continuations	--	---	--	+ 408,000
4. Research and development contracts	--	---	--	+ 200,000
Total, increases	--	---	--	+$17,741,000
Decreases:				
A. Program:				
1. Research grants:				
a. Noncompeting completed or converted to competing status	--	---	--	-$ 6,040,000
b. Competing completed or converted to noncompeting	--	---	--	- 8,126,000
c. 1974 obligations used to fund 1974 continuations	--	---	--	- 2,261,000

Decreases: (cont.)	1974 Pos.	1974 Amount	Change Pos.	Change Amount
2. Fellowships:				
a. Noncompeting completed or converted to competing status	--	---	--	-$ 305,000
b. Competing completed or converted to noncompeting	--	---	--	- 1,784,000
3. Training grants:				
a. Noncompeting completed or converted to competing status	--	---	--	- 1,863,000
b. Competing completed or converted to noncompeting	--	---	--	- 408,000
Total decreases	--	---	--	-$20,787,000
Total, Net Change	--	---	--	-$ 3,046,000

Explanation of Changes

Increases:

A. Built-in: These increases provide: (1) $42,000 for within-grade salary increases; (2) $5,000 for increased costs of using the Federal Tele-communicatives System; (3) $9,000 for an extra day of pay; (4) $3,000 for increased costs of Service and Supply; (5) $2,000 for an increase in payment to the Bureau of Employees Compensation; and (6) $141,000 for increased costs associated with the NIH Management Fund for centrally furnished services.

B. Program:

1. Research grants:
   a. The increase of $7,486,000 in noncompeting research grants represent the continuation of previously awarded grants plus "new" continuations resulting from grants made in 1974. The number of continuations increased by 27: from 276 in 1974 to 303 in 1975.

   b. The amount of $6,890,000 in competing research grants reflects: (1) $3,883,000 for 66 new awards; (2) $2,957,000 for 41 competing continuations; and (3) $50,000 in supplementals.

2. Fellowships:
   a. The increase of $1,784,000 in noncompeting fellowships represent the continuation of previously awarded fellowships plus "new" continuations resulting from fellowships made in 1974. The number of continuations increased by 93: from 30 in 1974 to 123 in 1975.

   b. The amount of $771,000 in competing fellowships reflects an increase of $771,000 for 53 new awards.

3. Training grants:
   a. The increase of $408,000 in noncompeting training grants represent the continuation of previously awarded training grants. The number of continuations decreased by 11, from 41 in 1974 to 30 in 1975.

Decreases: (cont.)

A. Program:

1. Research grants:
   a. The decrease of $6,040,000 represents 114 noncompeting regular research grants that were completed in 1974 or that are being converted to competing status in 1975.

   b. The decrease of $8,126,000 reflects the completion or conversion of 106 competing grants to a noncompeting status.

   c. The decrease of $2,261,000 reflects the reduced funding required in 1975 due to the multi-year funding of 35 projects in 1974.

2. Fellowships:
   a. The decrease of $305,000 represent 23 noncompeting fellowships that were completed in 1974 or that are being converted to competing status in 1975.

   b. The decrease of $1,784,000 reflects the completion or conversion of 116 competing fellowships to a noncompeting status.

3. Training grants:
   a. The decrease of $1,863,000 represent 19 noncompeting training grants that were completed in 1974 or that are being converted to competing status in 1975.

   b. The decrease of $408,000 reflects the completion or conversion of 8 competing training grants to a noncompeting status.

Obligations by Activity

Page Ref.		1974 Base* Pos.	1974 Base* Amount	1975 Estimate Pos.	1975 Estimate Amount	Increase or Decrease Pos.	Increase or Decrease Amount
107	Retinal and Choroidal diseases..............	--	$12,637,000 (13,683,000)	--	$12,534,000	--	-$103,000 A
109	Corneal diseases........	--	6,082,000 (6,651,000)	--	6,039,000	--	- 43,000 B
111	Cataract...............	--	2,987,000 (3,374,000)	--	2,987,000	--	---
113	Glaucoma...............	--	4,496,000 (4,946,000)	--	4,496,000	--	---
115	Sensory-motor disorders and rehabilitation.....	--	7,564,000 (8,097,000)	--	7,459,000	--	- 105,000 C
117	Intramural laboratory and clinical research..	73	4,323,000 (4,323,000)	73	4,458,000	--	+ 135,000 D
118	Research management and program services...	55	1,909,000 (1,919,000)	55	1,974,000	--	+ 65,000 E
	Total obligations (base)..........	128	$39,998,000	128	$39,947,000	--	- $51,000
	Total obligations...		($42,993,000)				

* 1974 Base-Excludes 1973 appropriation restorations.
Total obligations shown in parentheses.

Explanation of Changes (by activity)

A/ The Retinal and Choroidal diseases program decreased by $103,000, however, the Institute will be able to maintain a proper nucleus of research in diseases affecting the retina and the underlying vascular tissue.

B/ The Corneal diseases program was decreased by $43,000, which is approximately the same program level as 1974, however, the Institute will continue to place emphasis on reducing the impact of corneal diseases through improved methods of treatment, prevention, and diagnosis.

C/ The Sensory-Motor Disorders and Rehabilitation program was decreased by $105,000, however, the Institute will continue to support Laboratory and Clinical investigations on the development and function of those activities of the brain and the eye muscles which make vision possible.

D/ The increase of $135,000 for Intramural Laboratory and Clinical Research is made up as follows: $31,000 for built-in increases, $175,000 for payment to NIH Management Fund for centrally furnished services, offset by a $71,000 program reduction. Emphasis will be focused on disease processes and the function of visual systems.

E/ Research Management and Program Services is increased by $65,000. This increase represents $25,000 for built-in increases and a program increase of $40,000. Continued emphasis will be placed on insuring effective management of resources in order to consolidate and build upon the vision research accomplishments of the past.

Obligations by Object

	1974 Estimate	1975 Estimate	Increase or Decrease
Total number of permanent positions....................	128	128	---
Full-time equivalent of all other positions..............	8	8	---
Average number of all employees....................	123	123	---
Personnel compensation:			
Permanent positions...........	$2,053,000	$2,143,000	+$90,000
Positions other than permanent..................	113,000	120,000	+7,000
Other personnel compensation..	33,000	40,000	+7,000
Subtotal, personnel compensation.............	2,199,000	2,303,000	+104,000
Personnel benefits...........	260,000	270,000	+10,000
Travel and transportation of persons....................	129,000	139,000	+10,000
Transportation of things......	10,000	10,000	---
Rent, communications and utilities..................	65,000	70,000	+5,000
Printing and reproduction.....	13,000	26,000	+13,000
Other Services:			
Project contracts..........	2,122,000	2,322,000	+200,000
Payment to NIH Management Fund....................	2,606,000	2,781,000	+175,000
Other......................	960,000	808,000	-152,000
Supplies and materials........	243,000	262,000	+19,000
Equipment....................	232,000	250,000	+18,000
Grants, Subsidies, and contributions..............	34,154,000	30,706,000	-3,448,000
Total, obligations by object................	$42,993,000	$39,947,000	-$3,046,000
Total obligations excluding 1973 appropriation restorations.	$39,998,000	---	---

Significant Items in House and Senate Appropriations Committee Reports

Item	Action taken or to be taken
1974 Senate Report	
1. Because of the proposed funding level for fiscal year 1974, the Senate was very concerned that the Institute would be unable to exploit opportunities in glaucoma research, rehabilitation research, and medical research programs which would have a direct beneficial impact on eye care delivery and that basic research and research training programs would be at a level below that of 1971. Therefore, the Committee recommended a significant increase centering upon glaucoma, cataract, retinal degeneration and diabetic retinopathy and it felt that research efforts in the latter program should be one of inter-institute cooperations (page 57).	1. The 1974 funding increase will be used to expand research in glaucoma, cataract, retinal degeneration and diabetic retinopathy. Efforts will also be taken by the National Eye Institute to facilitate close cooperation with other Institutes on research into diabetic retinopathy.
2. The Committee was of the persuasion that grants and contracts for eye research should be awarded to small as well as large institutions (page 57).	2. The increased funding level will allow for additional grant support to small institutions. Also the implementation of a small research grants program to be initiated in FY 1974 designed especially for young investigators should allow smaller institutions to compete more favorably for grant support.

Authorizing Legislation

Legislation	Authorized	Appropriation requested
Public Health Service Act Section 301 -- Research and Investigations in General	Indefinite	$39,947,000
Title IV, Part F, -- National Eye Institute	Indefinite	

National Eye Institute

Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
1970 1/	$22,073,000	$22,073,000	$23,330,000	$22,652,000
1971	24,325,000	29,217,000	29,217,000	29,435,000
1972	31,258,000	34,437,000	38,404,000	35,670,000
1973*	33,797,000	36,809,000	43,247,000	36,809,000*
1974	32,092,000	36,631,000	46,631,000	41,682,000**
1975	39,947,000			

1/ Prior year appropriations were included within the National Institute of Neurological Diseases and Stroke.

*Note: This appropriation authority was the continuing resolution. The appropriation amount was the House Allowance, which was the lower of the House or Senate amounts in the first vetoed bill.

** Appropriation after reduction $39,998,000

Justification

National Eye Institute

	1974 Base*		1975 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits.........	128	$ 2,459,000	128	$ 2,573,000	---	+$114,000
Other expenses.........	---	37,539,000	---	37,374,000	---	-165,000
Total.............	128	$39,998,000	128	$39,947,000	---	-51,000

* Excludes 1973 appropriation restorations.

General Statement

The mission of the National Eye Institute is to conduct, foster, and support research and research training on the cause, natural history, prevention, diagnosis, and treatment of disorders of the eye, and the visual system. The objective of this research is to increase knowledge needed to deal with vision and vision-related health problems.

The extent of visual health problems in the United States is indicated by the facts that: (1) nearly 100,000,000 Americans have some form of eye disorder or impaired vision. Moreover, 370,000 Americans are unable to work, keep house, or engage in school or preschool activities because of visual impairments. (2) There are approximately 1.3 million Americans with visual handicaps severe enough to prevent them from reading ordinary newsprint, even with glasses. (3) An estimated 340,000 persons are legally blind and this number increases by approximately 30,000 new cases of blindness each year.

The resulting cost of rehabilitation, treatment, and maintenance payments, as well as lost productivity and income is enormous. This great loss of productivity and human resources indicates the need for a vigorous program of research on the care and rehabilitation of the visually disabled.

The National Eye Institute is the only organization within the Federal Government whose main concern is visual health. Therefore, if new advances in this field are to be fostered, they will result from initiatives supported by the NEI.

Research activities supported by the Institute are currently grouped under five major research areas: Retinal and Choroidal Diseases, Corneal Diseases, Cataract, Glaucoma, and Sensory-Motor Disorders and Rehabilitation. These programs encompass a multitude of vision research activities supported primarily through research grants, but complemented by a small contract program and an intramural research effort. To insure a continuous supply of trained manpower, in support of its programs, the Institute also awards research fellowships and training grants.

Institute scientists and grantees are engaged in research to advance understanding of vision and to attack the full range of those vision disorders affecting large segments of the population. These investigations have already contributed significantly to our knowledge of normal vision and to the development of more effective means for preventing, diagnosing and treating retinal disorders, corneal disease, glaucoma, cataracts, and inflammatory diseases of the eye.

Advances in vision research supported by the NEI have made significant inroads against visual disability and blindness in recent years. These have led to a shortening of hospitalization, a shift from inpatient to outpatient treatment, and a reduction in the costs of vocational rehabilitation or lifetime support. Some highlights are: (1) Cataract surgery has been made safer, easier, and more successful through several technical improvements made possible by NEI support; (2) recent research advances which suggest that the NEI is on the threshold of a scientific breakthrough that will allow these cataracts to be prevented medically and make possible great savings in hospitalization and surgical costs; (3) scientific findings which appear to point the way to improved medical care in glaucoma through early detection before loss of sight occurs; (4) an associated development which has made vitrectomy one of the most exciting new fields of eye surgery, with a significant potential for restoring sight to people blind from certain kinds of retinal detachment and vitreous disease, and (5) the use of soft contact lenses as an aid to healing and the relief of pain in corneal diseases has revolutionized the treatment of this significant cause of disability and lost productivity.

This year the Institute will continue to accelerate the application of recent research accomplishments to the prevention, diagnosis, and treatment of glaucoma, cataract, and retinal diseases. Specific objectives for FY 1975 are delineated under each program category.

DHEW - National Institutes of Health

CROSSWALK - 1974 COLUMN 1975 PRESIDENT'S BUDGET

INSTITUTE: National Eye Institute
(Dollars in thousand)

Mechanism / Program	Research Grants: Regular Program: Non-competing	Research Grants: Regular Program: Competing	Research Grants: Specials: Multi-disciplinary Centers	Research Grants: Specials: Other	Training Programs: Grants	Training Programs: Fellowships	Laboratory and Clinical Research	Research and Development Contracts	Other Direct Operations	Total
1974 Base Obligations										
1. Retinal & Choroidal Diseases	6,066	3,141		179	830	607		1,600	214	12,637
2. Corneal Diseases	3,372	1,513		81	606	213		250	47	6,082
3. Cataract	1,423	1,150		38	214	91		---	71	2,987
4. Glaucoma	2,179	998		49	674	229		272	95	4,496
5. Sensory-motor & Rehabilitation	4,094	2,179		152	579	512		---	48	7,564
6. Intramural Laboratory & Clinical Research							4,323			4,323
7. Research Management & Program Services									1,909	1,909
Subtotal......	17,134	8,981		499	2,903	1,652	4,323	2,122	2,384	39,998
Unobligated Balance Restored										
1. Retinal & Choroidal Diseases		496		32	426	92				1,046
2. Corneal Diseases		263		14	91	201				569
3. Cataract		145		6	157	79				387
4. Glaucoma		171		10	239	30				450
5. Sensory-motor & Rehabilitation		331		28	41	133				533
6. Intramural Laboratory & Clinical Research										
7. Research Management & Program Services									10	10
Subtotal......		1,406		90	954	535			10	2,995
Total Obligations.....	17,134	10,387		589	3,857	2,187	4,323	2,122	2,394	42,993

DHEW - National Institutes of Health

CROSSWALK - 1975 COLUMN 1975 PRESIDENT'S BUDGET

INSTITUTE: National Eye Institute
(Dollars in thousand)

Mechanism / Program	Research Grants									
	Regular Program		Specials		Training Programs		Laboratory and Clinical Research	Research and Development Contracts	Other Direct Operations	Total
	Non-competing	Competing	Multi-disciplinary Centers	Other	Grants	Fellowships				
1. Retinal & Choroidal Diseases	6,175	2,801		215	585	938		1,600	220	12,534
2. Corneal Diseases	3,552	1,210		97	386	446		300	48	6,039
3. Cataract	2,040	468		45	191	170			73	2,987
4. Glaucoma	2,034	1,063		61	439	379		422	98	4,496
5. Sensory-motor & Rehabilitation	4,769	1,348		181	393	720			48	7,459
6. Intramural Laboratory & Clinical Research							4,458			4,458
7. Research Management & Program Services									1,974	1,974
Total Obligations.....	18,570	6,890		599	1,994	2,653	4,458	2,322	2,461	39,947

National Eye Institute

Budget Mechanism

	1974*		1975	
	Number	Amount	Number	Amount
Grants				
Regular				
Non-competing................	276	$17,134,000	303	$18,570,000
Competing....................	59	4,301,000	41	2,957,000
New..........................	75	4,599,000	66	3,883,000
Supplemental.................	(5)	81,000	(4)	50,000
Subtotal.................	410	$26,115,000	410	$25,460,000
Special				
Research career program......	17	$439,000	19	$529,000
Scientific evaluation........	--	60,000	--	70,000
Subtotal.................	17	499,000	19	599,000
Total Grants....................	427	$26,614,000	429	$26,059,000
Fellowships				
Non-competing.................	30	$403,000	123	$1,882,000
Competing.....................	--	---	--	---
New...........................	81	1,249,000	53	771,000
Supplemental..................	--	---	--	---
Subtotal.................	111	$1,652,000	176	$2,653,000
Training Grants				
Non-competing.................	41	$2,903,000	30	$1,994,000
Competing.....................	--	---	--	---
New...........................	--	---	--	---
Supplemental..................	--	---	--	---
Subtotal.................	41	$2,903,000	30	$1,994,000
Laboratory & Clinical Research...		$4,323,000		$4,458,000
Research & Development Contracts.		2,122,000		2,322,000
Biometry, Epidemiology & Field Studies..................		475,000		487,000
Research Management & Program Services......................		1,909,000		1,974,000
Total.........................		$39,998,000		$39,947,000

* Excludes 1973 appropriation restorations.

Retinal and Choroidal Diseases

Authorizing Legislation: Public Health Service Act, Title IV, Part F

	1974 Base*		1975 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits..........	---	---	---	---	---	---
Other expenses.........	---	$12,637,000	---	$12,534,000	---	-$103,000
Total.............	---	$12,637,000	---	$12,534,000	---	-$103,000
Budget Mechanism:						
Research Grants:						
Regular.............	---	$ 9,207,000	---	$ 8,976,000	---	-$231,000
Special.............	---	179,000	---	215,000	---	+ 36,000
Subtotal..........	---	9,386,000	---	9,191,000	---	- 195,000
Fellowships...........	---	607,000	---	938,000	---	+ 331,000
Training Grants.......	---	830,000	---	585,000	---	- 245,000
Research & Development Contracts............	---	1,600,000	---	1,600,000	---	---
Biometry, Epidemiology & Field Studies......	---	214,000	---	220,000	---	+ 6,000
Total.........	---	$12,637,000	---	$12,534,000	---	-$103,000

* Excludes 1973 appropriation restorations.

Introduction: The retina program of the National Eye Institute supports research to acquire knowledge of how the retina responds to light and converts it into electrical signals that travel to the brain resulting in sight. Nourishing the retina, and attached to it, is the choroid. Since any abnormality of the choroid affects the retina, retinal and choroidal diseases are considered jointly by the Institute.

Program Plans for 1975: Major emphasis will be placed on increasing the base of scientific information required for an all-out clinical attack against several diseases of the retina. Examples include: studies to increase the resolution attainable with photographic methods such as fluorescent angiography, to provide information to assess the role of choroidal and retinal blood flow in many retinal diseases; the development of techniques for the quantitative measurement of choroidal and retinal blood flow; and carrying out studies on normal and diseased retinas in order to increase our knowledge of the biochemical changes which precede and accompany retinal disease.

In the area of diabetic retinopathy several clinical approaches will be stressed. These include the development and study of animal models of retinal disease to provide a sound basis for drug therapy and further understanding of human retinal function, and epidemiological studies to aid in determining factors responsible for retinal disease, as well as obtaining a more objective method for determining how much of the retina is functioning.

Accomplishments in 1974: During FY 1974 progress in research against retinal and choroidal diseases has been made in several areas: (a) a new method of measuring eye blood flow, providing a more reliable method of studying the alteration of blood flow to the retina which occurs in a number of diseases affecting that tissue; (b) the development of a technique which may allow clinicians to differentiate normal from abnormal blood circulation patterns behind the retina; (c) discovery that there is a congenital form of retrolental fibroplasia (RLF) identical to that form which occurs in premature infants who have received high oxygen therapy, a finding which indicates that factors other than oxygen in the hospital nursery may produce the typical pathologic changes in the retinal blood vessels which occur in this disease; and (d) development of an experimental scleral implant to be used in retinal detachment surgery which can be inflated or deflated with fluids during surgery and for several weeks thereafter which should be useful for the treatment of difficult cases.

Corneal Disease

Authorizing Legislation: Public Health Service Act, Title IV, Part F

	1974 Base*		1975 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits.........	---	---	---	---	---	---
Other expenses.........	---	$6,082,000	---	$6,039,000	---	-$43,000
Total.............	---	$6,082,000	---	$6,039,000	---	-$43,000

Budget Mechanism:

Research Grants:						
Regular............	---	$4,885,000	---	$4,762,000	---	-123,000
Special............	---	81,000	---	97,000	---	+ 16,000
Subtotal.........	---	4,966,000	---	4,859,000	---	-107,000
Fellowships..........	---	213,000	---	446,000	---	+233,000
Training Grants......	---	606,000	---	386,000	---	-220,000
Research & Development Contracts...........	---	250,000	---	300,000	---	+ 50,000
Biometry, Epidemiology & Field Studies.....	---	47,000	---	48,000	---	+ 1,000
Total........	---	$6,082,000	---	$6,039,000	---	-$43,000

* Excludes 1973 appropriation restorations.

Introduction: The Institute will support intensive research to advance knowledge on the structure and function of the cornea and to improve the diagnosis, treatment, and prevention of corneal disease. Diseases of the cornea, the transparent outer coat that covers the front of the eye are numerous. The most common corneal diseases are caused by viral infections and degenerative conditions. These disorders are the main causes of severe ocular pain and disability. Corneal disease, especially trachoma, are the main causes of blindness throughout the world. In this country trachoma is a particularly severe health problem among the rural poor and the American Indian population. Lacerations, radiation burns, and chemical burns account for a large proportion of the injuries to the cornea which cause permanent visual disability. It has been observed that corneal problems account for 25 percent of cases seen by ophthalmologists.

Program Plans for 1975: New drugs will be developed and tested for treatment of corneal viral infections. The usefulness of tissue-typing to improve the success rate in corneal transplantation will be further evaluated. An expanded effort on the biochemistry of corneal collagen will be pursued in an effort to understand how to prevent scar formation. Additionally, artifical tears and new devices to continuously deliver fluids and drugs to the eye will be developed.

Accomplishments in 1974: During FY 1974 studies conducted or supported by the National Eye Institute demonstrated that the shape of the cornea can be safely remolded by heat, offering new hope for victims of keratoconus (a condition in which the center of the cornea becomes conical in shape, causing reduced vision) and the possibility for correcting severe cases of nearsightedness and other optical conditions. In addition, continuing studies have provided for the development of an experimental blocking antibody treatment for donor corneas to inhibit the rejection of corneal grafts, thus providing a possible basis for protecting the transplanted tissue without systemic or topical use of potentially dangerous immunosuppressive drugs.

Cataract

Authorizing Legislation: Public Health Service Act, Title IV, Part F

	1974 Base*		1975 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits...........	---	---	---	---	---	---
Other expenses...........	---	$2,987,000	---	$2,987,000	---	
Total...............	---	$2,987,000	---	$2,987,000	---	---
Budget Mechanism:						
Research Grants:						
Regular..............	---	$2,573,000	---	$2,508,000	---	-$65,000
Special..............	---	38,000	---	45,000	---	+7,000
Subtotal...........	---	2,611,000	---	2,553,000	---	-58,000
Fellowships..........	---	91,000	---	170,000	---	+79,000
Training Grants......	---	214,000	---	191,000	---	-23,000
Biometry, Epidemiology & Field Studies.....	---	71,000	---	73,000	---	+2,000
Total........	---	$2,987,000	---	$2,987,000	---	---

* Excludes 1973 appropriation restorations.

Introduction: The NEI cataract program supports research in an effort to identify the causes of cataract and develop methods for its prevention and improved treatment. While the long term goal of the cataract program is the prevention of cataracts, the Institute has directed its efforts to more tangible objectives.

Program Plans for 1975: Research to be initiated or expanded in 1975 include: (a) the elucidation of the biology and chemistry of the normal human lens; (b) the development of better animal models for the study of human cataract; (c) the intensive study of all available animal models to explain cataract formation at the molecular level; (d) the study of the effect of factors outside the lens upon the development of cataract (such as drugs and nutrition); (e) the definition and classification of different types of cataract and the establishment of guidelines for the recognition of different kinds of cataract development; (f) the study of sugar cataract, such as those which occur in galactosemia and diabetes, both for improved understanding of more common types of lens opacities and for their importance in understanding the general disease states with which they are associated; (g) the conduct of epidemiological studies to determine what factors may increase one's risk to developing cataract; (h) stressing the training of ophthalmologists in an environment that encourages an exposure to the basic sciences. This exposure should provide these clinicians a well-balanced orientation in the physiology and chemistry of the normal and cataractous lens as well as orientation in clinical aspects of the disease.

Accomplishments in 1974: Aggregation of lens proteins has been shown to simulate the loss of transparency in senile cataract. In addition, this aggregation can be reversed in the test tube so that a solution of protein once again becomes transparent. These findings have acted as an impetus in studies of cataract formation. In another type of cataract, the recent progress made in first inducing, then delaying the formation of sugar cataracts in experimental animals has provided an opportunity for finding more effective inhibitors of the enzyme aldose reductase capable of completely blocking lens changes in living animals. Since there may be a similarity between sugar cataract and other metabolic and congenital cataracts, a recently developed strain of mice with congenital cataract will facilitate studies of this relationship. The significance of these findings regarding sugar and congenital cataracts to research on slow developing senile cataracts needs to be explored.

Other recent accomplishments in this area include: (a) the discovery of many new cataractogenic drugs supposedly with different mechanisms for producing cataract which could increase the scope of available animal models for cataract; (b) the development of methods for studying the transparency of the lens utilizing laser and x-ray techniques; and (c) the development of techniques to measure changes in the transparency, in human or animal lenses. Such methods will facilitate the classification of cataract and the observation of the changes in transparency which occur with cataract development, hopefully providing some clues to the causation of cataracts.

Glaucoma

Authorizing Legislation: Public Health Service Act, Title IV, Part F

	1974 Base*		1975 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits..........	---	---	---	---	---	---
Other expenses..........	---	$4,496,000	---	$4,496,000	---	---
Total..............	---	$4,496,000	---	$4,496,000	---	---
Budget Mechanism:						
Research Grants:						
Regular.............	---	$3,177,000	---	$3,097,000	---	-$ 80,000
Special.............	---	49,000	---	61,000	---	+ 12,000
Subtotal..........	---	3,226,000	---	3,158,000	---	- 68,000
Fellowships.........	---	229,000	---	379,000	---	+ 150,000
Training Grants.....	---	674,000	---	439,000	---	- 235,000
Research & Development Contracts	---	272,000	---	422,000	---	+ 150,000
Biometry, Epidemiology & Field Studies....	---	95,000	---	98,000	---	+ 3,000
Total.......	---	$4,496,000	---	$4,496,000	---	---

* Excludes 1973 appropriation restorations.

Introduction: Glaucoma is a group of diseases characterized by loss of visual function associated with increased pressure within the eye. The National Eye Institute glaucoma program supports research on the cause of glaucoma, development of prevention and detection techniques, and improved methods of treatment.

Program Plans for 1975: The Institute will continue to support studies to develop better means for early detection, particularly the identification of the "glaucoma-prone" individual. Studies will also be conducted on: (a) the classification of the steroid-response mechanism in otherwise healthy individuals, which may lead to a test for glaucoma susceptibility and provide new insights into the nature of the disease, (b) photographs of certain unique markings on the retina which indicate that it may be possible to evaluate accurately and quickly the presence and extent of visual loss from glaucoma (this procedure at present is time-consuming and difficult), (c) a technique for widespread screening of large populations for early signs of glaucoma, and (d) the increase in the vertical dimension of a portion of the optic nerve, which can be easily visualized, to identify the early presence of glaucoma.

In addition, population studies to determine the factors which place a person at high risk to developing glaucoma will be conducted. Racial, ethnic, and other demographic aspects of the disease will be determined through well-designed epidemiological studies. The action of current glaucoma drugs for medical treatment will be explored, and new drugs will be developed for those cases presently resistant to drug therapy. New methods of glaucoma surgery, the last resort when drugs fail to control pressure, involving cryosurgery, miniaturized instruments for microsurgery, lasers, and enzymes which could open up new outflow channels, will be developed and evaluated in experimental animals.

Accomplishments in 1974: Important studies were conducted on the pathophysiology of aqueous production and outflow in glaucoma, the relationships between ocular hypertension and the circulation of blood in the retina and choroid, and the localization of the primary site of resistance to aqueous outflow in glaucoma: the inner lining of Schlemm's canal.

In addition, animal studies determined that the drug, diphenylhydantoin, commonly used to control seizures in epilepsy, can partially reverse the effects of oxygen deprivation in nerve cells, including those of the optic nerve. Because oxygen deprivation may be the result of increased pressure and the immediate cause of visual loss in glaucoma, this finding indicates for the first time the possibility that the effects of glaucoma may be reversed.

Sensory-Motor Disorders and Rehabilitation

Authorizing Legislation: Public Health Service Act, Title IV, Part F

	1974 Base*		1975 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits..........	---	---	---	---	---	---
Other expenses.........	---	$7,564,000	---	$7,459,000	---	-$105,000
Total.............	---	$7,564,000	---	$7,459,000	---	-$105,000

Budget Mechanism:

	1974 Base*		1975 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Research Grants:						
Regular............	---	$6,273,000	---	$6,117,000	---	-$156,000
Special............	---	152,000	---	181,000	---	+ 29,000
Subtotal..........	---	6,425,000	---	6,298,000	---	- 127,000
Fellowships.........	---	512,000	---	720,000	---	+ 208,000
Training Grants.....	---	579,000	---	393,000	---	- 186,000
Biometry, Epidemiology & Field Studies....	---	48,000	---	48,000	---	---
Total.......	---	$7,564,000	---	$7,459,000	---	-$105,000

* Excludes 1973 appropriation restorations.

Introduction: The sensory-motor program of the NEI supports laboratory and clinical investigations of the optic nerve and the development and function of those activities of the brain and the eye muscles which make vision possible.

Program Plans for 1975: Studies on the organization and failure of the visual system in the higher neural centers will continue in the coming year. Degenerative disease and other disorders of the optic nerve, which account for almost 10% of the cases of legal blindness in America, will be studied from the standpoints of etiology, early diagnosis, and treatment. The neuroanatomical and neurophysiological studies to be supported are expected to inform us of the path of visual information through the brain and the pathologic alterations of that path resulting from visual deprivation, injury, or dysfunction. These investigations will complement those on the function of the ocular muscles and their neural control which insures optimum presentation of visual stimuli to the retina. Furthermore, the anticipated increase in our understanding of the neural architecture of the visual system will eventally permit the development of improved vision therapy for victims of brain damage or congenital abnormalities.

The Institute will continue to support the development of improved diagnostic techniques for detection of refractive error, strabismus, and amblyopia, particularly in young patients where the possibility of permanent damage from uncorrected defects is greatest.

Finally, NEI supported studies will continue to provide new knowledge for improved contact lens design and a greater understanding of the psychophysical correspondence between the senses to permit useful substitution of another sense for lost vision in the development of visual prostheses.

Accomplishments in 1974: During FY 1974 investigators supported by the National Eye Institute have continued to explore both the normal physiology and architecture of the visual system under normal and abnormal conditions. Such studies in the monkey have shown that the critical period for visual development is the first six weeks of life. Visual deprivation during this period leads to permanent loss of visual acuity.

For the human infant, diagnosis of visual impairment during this critical period is essential. Therefore, the Institute is supporting the development of diagnostic procedures which permit the identification of amblyopia before it research a dysfunctional level.

New information has been reported of how the brain controls eye movements which improve our understanding of disorders in which a defect in this mechanism causes visual disability.

A new technique for tracing the nerve pathways from the eyes to the brain by using highly specific radioactive tracers which permit the visualization of labeled nerve cells under the microscope has been developed. This accomplishment is expected to have a major impact on studies of the structure of all parts of the nervous system in health and disease.

Finally, progress has been continued in the development of a lightweight, portable seeing aid for the totally blind. Experienced blind subjects using the aid can now distinguish objects, "read" large symbols, and identify persons in their vicinity by hair length and other cues.

Intramural Laboratory and Clinical Research

Authorizing Legislation: Public Health Service Act, Title IV, Part F

	1974 Base*		1975 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits..........	73	$1,404,000	73	$1,471,000	---	+$67,000
Other expenses..........	---	2,919,000	---	2,987,000	---	+ 68,000
Total..............	73	$4,323,000	73	$4,458,000	---	+$135,000

* Excludes 1973 appropriation restorations.

Introduction: The National Eye Institute's intramural research program is a great national resource. The wide range of research interests being pursued at the reservation in Bethesda by all of the research institutes provides the capability for a multi-disciplinary approach to vision research not available elsewhere in the world. This program is focused on developing new and improved techniques for the prevention, diagnosis, and treatment of vision disorders.

Program Plans for 1975: The Laboratory of Vision Research will continue to develop areas of research that will provide better insight into disease processes and the function of visual systems. Because of the paucity of information regarding disease processes greater emphasis will be placed in this area. Animal models to study retinitis pigmentosa will be used to determine the primary event that triggers the process of this retinal dystrophy. Biochemical and immunological studies will be conducted to determine if there are specific protein antigens in the cornea that are responsible for cornea graft rejections. Since Laboratory of Vision Research scientists have uncovered the basic mechanisms that are involved in cataracts associated with diabetes and galactosemia, it is now possible, in animals, to delay the onset of these cataracts with chemical agents. Follow-up experiments for effecting delay or prevention of cataracts based on these developments will be explored. Objectives of the Clinical Branch in FY 1975 include: a study of patients with ocular melanomas (tumors) to develop improved methods of diagnosis and treatment; a study of retinal function in various forms of retinitis pigmentosa and related diseases in an effort to arrive at more precise diagnostic criteria and prognosis; a study of patients who have undergone immunologic rejection of corneal grafts to determine the relationship of the development of antibodies against the antigens of the donor when the corneas are regrafted; the problem of new vessel formation and vitreous hemorrhage will be attacked by the development of improved instruments using ultrasonic driven cutters to remove strands of vitreous humor.

Accomplishments in 1974: During FY 1974, the intramural research program continued to emphasize clinical studies on diseases of the retina and cornea, glaucoma, and cataract. Studies included the evaluation of the use of soft contact lens in treating corneal diseases and improving the comfort of patients with such disorders. Studies were also continued to learn whether the success rate of corneal transplantation could be improved by the antigenic matching of donors and recipients. Investigations into vascular disease, including diabetic retinopathy, macular degeneration, and inherited retinal disorders were also conducted. Additionally, intramural scientists played a crucial role in the scientific management and evaluation of the Institute's major programs.

Research Management and Program Services

Authorizing Legislation: Public Health Service Act, Title IV, Part F

	1974 Base*		1975 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits..........	55	$ 568,000	55	$ 595,000	---	+$27,000
Other expenses..........	--	1,341,000	--	1,379,000	---	+ 38,000
Total.............	55	$1,909,000	55	$1,974,000	---	+$65,000

* Excludes 1973 appropriation restorations.

Introduction: This program provides support for the Office of the Director, NEI, which has responsibility for overall administrative management and scientific direction of Institute programs. Funds are also provided for salaries and other expenses of the Office of the Associate Director for Extramural and Collaborative Programs.

Program Plan for 1975: Program planning, analysis and evaluation activities carried out in concert with the National Advisory Eye Council will receive greater emphasis in 1975. Recommendations of the Council for achieving program balance and providing guidance as to future directions of the Institute will be evaluated and implemented where appropriate. Continued emphasis will be placed on insuring effective management of limited resources in order to consolidate and build upon the research accomplishments of the past supported by the Institute.

Accomplishments in 1974: During FY 1974, this program will be engaged in applying the six NEI objectives established for the program budget as the basis for planning and evaluating all NEI programs. Staff offices are working to coordinate the collection and dissemination of grant and contract information on a program rather than a mechanism basis. Staff members and outside experts are collaborating with a recently-established planning subcommittee to the National Advisory Eye Council to discuss methods of achieving program balance and recommending future directions for NEI supported vision research.

The functions of the Office of Scientific Reports and Program Coordination have been expanded to include all program planning activities for the Institute. This Office has also begun to document the long-term vision research accomplishments supported by NEI and has provided support services for the planning and evaluation activities of the National Advisory Eye Council.

The Office of Extramural and Collaborative Programs is working to develop a more sophisticated and responsive computer-based information system which will produce information relative to grants and contracts on a program basis. In addition to providing overall leadership to the Institute, the Office of the Director is currently engaged in the planning stage of a proposed U.S.-Japan vision research program.

NATIONAL INSTITUTES OF HEALTH

National Eye Institute

Program Purpose and Accomplishments

Activity: Retinal and Choroidal Diseases
(Public Health Service Act, Title IV, Part F)

1974		1975		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
--	$12,637,000	Indefinite	--	$12,534,000

Purpose: The retina program of the National Eye Institute supports research to obtain a better understanding of how the retina responds to light and converts it into electrical signals that travel to the brain resulting in sight. It also includes research to advance understanding of how the retina is damaged by disease, to develop methods of prevention, early detection, and treatment of retinal disease; and development of animal models of various retinal diseases to facilitate laboratory and clinical research.

Explanation: This program is supported through the awarding of research and training grants to universities and other non-profit institutions, the awarding of fellowships to individuals, research and development contracts, and studies conducted by the Office of Biometry and Epidemiology.

Accomplishments in 1974: Innovations in research against retinal and choroidal diseases have produced the following: (a) a new method of measuring ocular blood flow using radioactive plastic microspheres, (b) a technique which may allow clinicians to differentiate normal from abnormal blood circulation patterns behind the retina; (c) finding that there is a congenital form of retrolental fibroplasia (RLF) identical to that which occurs in premature infants who have received high oxygen therapy; (d) development of an experimental scleral implant to be used in retinal detachment surgery.

Objectives for 1975: Experimental aspects that will be studied relate to: (a) the transfer of nutrients between the choroid and retina, (b) increasing the ability to assess photographically the role of choroidal and retinal blood flow, (c) inherited retinal dystrophies, particularly, retinitis pigmentosa, (d) studies on normal and diseased retinas in order to increase our knowledge of the biochemical changes associated with retinal disease.

Several new approaches will be taken in order to discover the cause of diabetic retinopathy and other circulatory disorders of the retina, including the development and study of animal models, and epidemiological studies to determine risk factors associated with retinal disease.

NATIONAL INSTITUTES OF HEALTH

National Eye Institute

Program Purpose and Accomplishments

Activity: Corneal Diseases
(Public Health Service Act, Title IV, Part F)

1974			1975	
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
--	$6,082,000	Indefinite	--	$6,039,000

Purpose: The NEI corneal disease program is aimed at reducing the impact of this leading cause of visual disability through improved methods of treatment, prevention, and diagnosis.

Explanation: This program is supported through the awarding of research and training grants to universities and other non-profit institutions, the awarding of fellowships to individuals, research and development contracts, and studies conducted by the Office of Biometry and Epidemiology.

Accomplishments in 1974: Studies conducted or supported by the National Eye Institute demonstrate that the shape of the cornea can be safely remolded by heat, offering new hope for victims of keratoconus (a condition where the center of the cornea becomes conical in shape, causing reduced vision) and the possibility of correcting severe cases of nearsightedness and other optical conditions. In addition, continuing studies have provided leads for the further development of an experimental blocking antibody treatment for donor corneas to inhibit the rejection of corneal grafts, without systemic or topical use of potentially dangerous immunosuppressive drugs.

Objectives for 1975: The Institute will support intensive research to advance knowledge on the structure and function of the cornea and to improve the diagnosis, treatment, and prevention of corneal disease.

New drugs and interferon will be developed and tested for treatment of corneal viral infection. The usefulness of tissue-typing to improve the success rate in corneal transplantation will be evaluated. An expanded effort on the biochemistry of corneal collagen will be pursued in an effort to understand how to prevent scar formation. Artificial tears and new devices to continuously deliver fluids and drugs to the eye will be further developed.

NATIONAL INSTITUTES OF HEALTH

National Eye Institute

Program Purpose and Accomplishments

Activity: Cataracts (Public Health Service Act, Title IV, Part F)

1974		1975		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
--	$2,987,000	Indefinite	--	$2,987,000

Purpose: A cataract is a cloudiness or opacity in the lens of the eye, which interferes with the transmission of light to the retina. The NEI cataract program supports research to identify the causes of this disorder and develop methods for its prevention and improved treatment.

Explanation: This program is supported through the awarding of research and training grants to universities and other non-profit institutions, the awarding of fellowships to individuals, research and development contracts, and studies conducted by the Office of Biometry and Epidemiology.

Accomplishments in 1974: Through National Eye Institute research, the inhibitor of an enzyme which has been found to trigger sugar cataract has been identified and used to prevent this type of cataract in the test tube and delay its formation in living animals. Tests of a new hypothesis of senile cataract formation has led to the induction and subsequent reversal of a cataract in the test tube. A number of new techniques are currently in various stages of development using suction, along with a means for breaking up the lens, for cataract removal in older people.

Other recent accomplishments in this area include: (a) the discovery of many new cataractogenic drugs supposedly with different mechanisms for inducing cataract, (b) the development of methods for studying the transparency of the lens utilizing laser and x-ray techniques, and (c) the development of techniques to measure changes in the transparency of human or animal lenses.

Objectives for 1975: Specific objectives to be initiated or expanded in FY 1975 include: (a) the elucidation of the biology and chemistry of the normal human lens, (b) the development of better animal models for the study of human cataract, (c) the study of the effect of factors outside the lens upon the development of cataract, (d) the definition and classification of different types of cataracts, (e) the study of sugar cataracts for improved understanding of more common types of lens opacities, and (f) the conduct of epidemiological studies to determine what factors may increase one's risk of developing cataract.

NATIONAL INSTITUTES OF HEALTH

National Eye Institute

Program Purpose and Accomplishments

Activity: Glaucoma (Public Health Service Act, Title IV, Part F)

1974		1975		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
--	$4,496,000	Indefinite	--	$4,496,000

Purpose: Glaucoma is a group of diseases characterized by loss of visual function associated with damage to the optic nerve and increased pressure within the eye. The NEI glaucoma program supports research on the cause of glaucoma, development of techniques for prevention and early detection of the disease, and improved methods of treatment.

Explanation: This program is supported through the awarding of research and training grants to universities and other non-profit institutions, the awarding of fellowships to individuals, research and development contracts, and studies conducted by the Office of Biometry and Epidemiology.

Accomplishments in 1974: Studies were conducted on the pathophysiology of aqueous production and outflow in glaucoma. Relationships were determined between ocular hypertension and the circulation of blood in the retina and choroid, and the localization of the primary site of resistance to aqueous outflow in glaucoma.

Animal studies demonstrated that the drug diphenylhydantoin can partially reverse the effects of oxygen deprivation in nerve cells.

Objectives for 1975: The Institute will continue support of studies to develop better means of early detection, including further investigation of the steroid-response mechanism, the possibility of evaluating visual loss from glaucoma through simple photography, and identifying the early presence of the disease by examining the vertical dimensions of the optic nerve.

Epidemiological investigations will be conducted to identify risk factors associated with glaucoma. Studies will be conducted to assess current glaucoma drugs for improved medical treatment, and new drugs will be developed for those cases presently resistant to drug therapy. New methods of glaucoma surgery will be developed and evaluated in experimental animals.

NATIONAL INSTITUTES OF HEALTH

National Eye Institute

Program Purpose and Accomplishments

Activity: Sensory-Motor Disorders and Rehabilitation (Public Health Service Act, Title IV, Part F)

1974		1975		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
---	$7,564,000	Indefinite	---	$7,459,000

Purpose: The sensory-motor program of the National Eye Institute supports laboratory and clinical investigations of the optic nerve and the development and function of those activities of the brain and the eye muscles which make vision possible. Support is also provided for the development of rehabilitation techniques and vision substitution devices.

Explanation: This program is supported through the awarding of research and training grants to universities and other non-profit institutions, the awarding of fellowships to individuals, research and development contracts, and studies conducted by the Office of Biometry and Epidemiology.

Accomplishments in 1974: Studies on the development of the visual system under normal and abnormal conditions were conducted. Such studies in the monkey have shown that the critical period for visual development is the first six weeks of life, and that visual deprivation during this period may lead to permanent loss of visual acuity.

The Institute is supporting the development of diagnostic procedures which will permit the identification of amblyopia before it interfers with vision. A new technique for tracing nerve pathways from the eye to the brain using radioactive tracers has also been developed.

Objectives for 1975: Degenerative disease and other disorders of the optic nerve will be studied from the standpoints of etiology, early diagnosis, and treatment. In addition, NEI-supported studies will seek knowledge and understanding of the correspondence between the senses to permit useful substitution of another sense for lost vision in the development of visual prostheses.

NATIONAL INSTITUTES OF HEALTH

National Eye Institute

Program Purpose and Accomplishments

Activity: Intramural Laboratory and Clinical Research (Public Health Service Act, Title IV, Part F)

1974			1975 Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
73	$4,323,000	Indefinite	73	$4,458,000

Purpose: The intramural laboratory and clinical research program of the National Eye Institute is focused on developing new and improved techniques for the prevention, diagnosis, and treatment of vision disorders.

Explanation: The Institute's intramural research program is comprised of a Laboratory of Vision Research which conducts studies on the fundamental disease processes of the eye and structure and function of the visual system, and a Clinical Branch which applies laboratory knowledge to improved health care and the prevention of visual disorders.

Accomplishments in 1974: The NEI continued to emphasize clinical studies on diseases of the retina and cornea, glaucoma, and cataract. Studies included the evaluation of the use of soft contact lens in treating corneal diseases, and improving the comfort of patients with such disorders. Studies were conducted to learn whether the success rate of corneal transplantation could be improved by the antigenic matching of donors and recipients. Investigations into vascular disease, including diabetic retinopathy, macular degeneration, and inherited retinal disorders were also conducted. Additionally, intramural scientists played a crucial role in the management and evaluation of the Institute's major program areas.

Objectives for 1975: The Laboratory of Vision Research will continue to develop areas of research that will provide better insight into disease processes and function of visual systems. Research will be conducted on animal models to study retinitis pigmentosa to determine the primary event that triggers the process of this retinal dystrophy. Biochemical and immunological studies will be conducted on protein antigens in the cornea that are responsible for cornea graft rejections. Follow-up experiments for effecting delay or prevention of cataracts will be explored. Objectives of the Clinical Branch include: a study of patients with ocular melanomas (tumors); a study of retinal function in various forms of retinitis pigmentosa and related diseases; a study of patients who have undergone immunologic rejection of corneal grants; a study to determine the relationship of the development of antibodies against the antigens on the donor when the corneas are regrafted; a study of the problem of new vessel formation and vitreous hemorrhage.

Additionally, the Clinical Branch will continue collaborative studies on several protocols originated in other institutes, i.e., the systematic documentation of diabetic retinopathy in the Pima Indians diabetes study of the National Institute of Arthritis, Metabolism and Digestive Diseases.

NATIONAL INSTITUTES OF HEALTH

National Eye Institute

Program Purpose and Accomplishments

Activity: Research Management and
Program Services (Public Health Service Act, Title IV, Part F)

1974			1975	
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
55	$1,909,000	Indefinite	55	$1,974,000

Purpose: This program provides support for the Office of the Director, National Eye Institute, which has responsibility for overall administrative management and scientific direction of Institute programs. Funds are also provided for salaries and other expenses of the Office of the Associate Director for Extramural and Collaborative Programs.

Explanation: This office is responsible for the managememt of research grant, fellowship and training grant programs sponsored by the Institute, for the development and implementation of contract supported research programs, and the overall direction of the direct research programs of the Institute.

Accomplishments in 1974: After determining NEI program objectives for the program budget structure, this program has been engaged in utilizing the objectives established for the program budget as the basis for planning and evaluating all NEI programs. Staff offices are working to coordinate the collection and dissemination of grant and contract information on a program rather than a mechanism basis. Staff members and outside experts are collaborating with a recently-established planning subcommittee to the National Advisory Eye Council (NAEC) to discuss methods of achieving program balance and recommending future directions for NEI supported vision research.

The functions of the Office of Scientific Reports and Program Coordination have been expanded to include all program planning activities such as the coordination of the "Annual Report" (which is the major source of data on intramural programs), the "blueprint" of NEI activities, and the five-year plan. This Office has also initiated a documentation of long-term vision research accomplishments supported by NEI and has provided support services for the planning and evaluation activities of the National Advisory Eye Council.

The role of health scientist administrators within the office of extramural and collaborative programs have been expanded to serve as focal points for information for their respective program areas. The Office of the Director is engaged in the planning stages of a proposed U.S-Japan vision research program. In addition, these offices have continue to provide the administrative guidance and program direction necessary for the day-to-day operation of the NEI.

Objectives for 1975: Program planning, analysis and evaluation activities carried out in concert with the National Advisory Eye Council (NAEC) will be continued and expanded in 1975. Recommendations of the Council for achieving program balance and providing guidance as to future directions of the Institute will be evaluated and implemented where appropriate. Continued emphasis will be placed on insuring effective management of resources in order to consolidate and build upon the vision research accomplishments of the past.

TUESDAY, APRIL 2, 1974.

NATIONAL LIBRARY OF MEDICINE

WITNESSES

DR. MARTIN M. CUMMINGS, DIRECTOR
DR. ROBERT S. STONE, DIRECTOR, NATIONAL INSTITUTES OF HEALTH
MELVIN S. DAY, DEPUTY DIRECTOR, NATIONAL LIBRARY OF MEDICINE
KENT A. SMITH, ASSISTANT DIRECTOR FOR ADMINISTRATION, NATIONAL LIBRARY OF MEDICINE
FRANK B. POH, FINANCIAL MANAGEMENT OFFICER, NATIONAL LIBRARY OF MEDICINE
LEON M. SCHWARTZ, ASSOCIATE DIRECTOR FOR ADMINISTRATION, NATIONAL INSTITUTES OF HEALTH
LELAND B. MAY, ACTING DIRECTOR OF FINANCIAL MANAGEMENT, NATIONAL INSTITUTES OF HEALTH
DR. ERNEST ALLEN, ASSOCIATE DIRECTOR, EXTRAMURAL PROGRAM, NATIONAL LIBRARY OF MEDICINE
CHARLES MILLER, DEPUTY ASSISTANT SECRETARY, BUDGET

Object Classification (in thousands of dollars)

Identification code 09-25-0807-0-1-651		1973 actual	1974 est.	1975 est.
	Direct obligations:			
	Personnel compensation:			
11.1	Permanent positions	7,183	7,762	8,225
11.3	Positions other than permanent	290	335	333
11.5	Other personnel compensation	104	104	104
11.8	Special personal services payments			
	Total personnel compensation	7,577	8,201	8,662
12.1	Personnel benefits: Civilian	671	727	772
21.0	Travel and transportation of persons	176	175	180
22.0	Transportation of things	18	26	34
23.0	Rent, communications, and utilities	1,755	1,862	1,960
24.0	Printing and reproduction	419	464	499
25.0	Other services	6,735	9,003	8,116
26.0	Supplies and materials	258	271	298
31.0	Equipment	706	1,412	935
41.0	Grants, subsidies, and contributions	6,649	7,689	6,282
	Total direct obligations	24,964	29,830	27,738
	Reimbursable obligations:			
21.0	Travel and transportation of persons	40	40	50
22.0	Transportation of things	1	---------	---------
23.0	Rent, communications, and utilities	29	35	40
25.0	Other services	864	1,065	1,330
26.0	Supplies and materials	48	50	60
31.0	Equipment	5	10	20
	Total reimbursable obligations	969	1,200	1,500
99.0	Total obligations	25,933	31,030	29,238

Personnel Summary

	1973 actual	1974 est.	1975 est.
Total number of permanent positions	473	461	460
Full-time equivalent of other positions	24	26	24
Average paid employment	496	500	499
Average GS grade	8.5	8.6	8.6
Average GS salary	$14,260	$15,138	$15,473
Average salary of ungraded positions	$11,138	$12,018	$12,253

Program and Financing (in thousands of dollars)

	Identification code 09-25-0807-0-1-651	1973 actual	1974 est.	1975 est.
	Program by activities:			
	Direct program:			
	1. Medical library assistance	8,435	7,689	6,282
	2. Direct operations:			
	Lister Hill National Center for Biomedical Communications	2,125	2,752	2,572
	National Medical Audiovisual Center	2,671	3,326	2,816
	Library operations	9,205	9,754	9,734
	Toxicology information	1,591	1,813	1,808
	Research management and program services	4,278	4,496	4,526
	Total direct program	28,305	29,830	27,738
	Reimbursable program:			
	National Medical Audiovisual Center	871	1,100	1,350
	Library operations	98	100	150
	Total reimbursable program	969	1,200	1,500
	Total program costs, funded [1]	29,274	31,030	29,238
	Change in selected resources (undelivered orders)	−3,341		
10	Total obligations	25,933	31,030	29,238
	Financing:			
11	Receipts and reimbursements from: Federal funds	−969	−1,200	−1,500
21	Unobligated balance available, start of year	−55	−27	
24	Unobligated balance available, end of year	27		
25	Unobligated balance lapsing	3,632		
	Unobligated balance restored		−3,494	
	Budget authority	28,568	26,309	27,738
	Budget authority:			
40	Appropriation	28,568	25,871	27,738
41	Transferred to other accounts		−20	
43	Appropriation (adjusted)	28,568	25,851	27,738
46.20	Proposed transfer for civilian pay raises		458	
	Relation of obligations to outlays:			
71	Obligations incurred, net	24,964	29,830	27,738
72	Obligated balance, start of year	18,885	18,342	16,376
74	Obligated balance, end of year	−18,342	−16,376	−12,410
77	Adjustments in expired accounts	−489		
90	Outlays, excluding pay raise supplemental	25,018	31,338	31,704
91.20	Outlays from civilian pay raise supplemental		458	

[1] Includes capital outlay as follows: 1973, $706 thousand; 1974, $1,412 thousand 1975, $935 thousand.

NOTES

Includes $12 thousand in 1975 for activities previously financed from: National Institute of General Medical Sciences, 1973, $10 thousand; 1974, $10 thousand.

Excludes $66 thousand in 1975 for activities transferred to the Office of the Assistant Secretary for Health. Comparable amounts for 1973 ($66 thousand), 1974 ($66 thousand) are included above.

Excludes $20 thousand in 1974 and 1975 for activities transferred to Departmental Management. Comparable amount for 1973 ($20 thousand) is included above.

Mr. Flood. Now we have the National Library of Medicine and the presentation will be made by Dr. Martin M. Cummings, director.

We will place your biographical sketch in the record, Dr. Cummings, and others.

[The biographical sketch follows:]

Biographical Sketch

Name.—Martin Marc Cummings
Position.—Director, National Library of Medicine
Birthplace and date.—Camden, N.J., September 7, 1920
Education.—B.S., Bucknell University, 1941; M.D., Duke University, 1944
Experience

Present—Director, National Library of Medicine; 1963–64—Associate Director for Research Grants, National Institutes of Health; 1961–63—Chief, Office of International Research, National Institutes of Health; 1959–61—Professor of microbiology and chairman, Department of Microbiology, University of Oklahoma School of Medicine; 1953–59—Director, Research Services, Veterans' Administration Central Office; 1953–59—Special lecturer in microbiology, George Washington University School of Medicine; 1953—Associate professor of bacteriology, Emory University; 1949–53—Chief, Tuberculosis Research Laboratory, Veterans' Administration Hospital of Atlanta; 1948–53—Instructor through associate professor of Medicine, Emory University; 1947–49—Director, Tuberculosis Evaluation Laboratory, Communicable Disease Center, U.S. Public Health Service; 1945–49—Assistant Resident, Boston Marine Hospital; 1944–45—Intern, Boston Hospital; 1942–44—U.S. Army, Pfc.

Association memberships

American Academy of Microbiology, Inc.; American Board of Microbiology; American Federation for Clinical Research (emeritus); American Society for Clinical Investigation (emeritus); Association for American Medical Colleges; Medical Library Association; Society of Sigma XI; American Clinical and Climatological Association; American Society for the History of Medicine; board of directors, Gorgas Memorial Foundation; American Documentation Institute; Association of Research Libraries; Society of Medical Administrators.

Special awards, citations, or publications

Veterans' Administration Exceptional Service Medal; DHEW Superior Service Award; DHEW Distinguished Service Award; honorary doctor of science, Bucknell University, 1969; Distinguished Alumnus Award, Duke University; Honorary doctor of science, University of Nebraska, 1971; honorary doctor of science, Emory University, 1971; honorary doctor of humane letters, Georgetown, 1971; honorary member, Alpha Omega Alpha; honorary doctor of medicine, Karolinska Institute, Stockholm, Sweden, 1972; honorary fellowship. College of Physicians, Philadelphia, 1973; Rockefeller Public Service Award, 1973.

Biographical Sketch

Name.—Melvin Sherman Day
Position.—Deputy Director, National Library of Medicine.
Birthplace and date.—Lewiston, Maine, January 22, 1923
Education.—B.S., Bates College, Lewiston, Maine, 1943
Experience.

Present—Deputy Director, National Library of Medicine; 1971–72—Head, Office of Science Information Service, National Science Foundation; 1966–71—Deputy Assistant Administrator for Technology Utilization. NASA Headquarters; 1962–66—Director, Scientific and Technical Information Division, NASA Headquarters; 1958–60—Director. Division of Technical Information, Extension. AEC; 1955–56—Assistant Chief, Technical Information Extension, AEC; 1952–55—Operations Officer, Technical Information Services, AEC; 1948–52—Physical Science Information Editor, Technical Information Service, AEC; 1946–48—Chemist, Technical Information Division. Atomic Energy Commission; 1944–46—U.S. Army Corps of Engineers and served as laboratory foreman (chemist), U.S. Army, Eastman Kodak Corp.; 1943–44—Chemist, Metal Hydrides Inc.

Association Memberships.

American Association for the Advancement of Science; New York Academy of Sciences; American Chemical Society; American Society of Information Science; Special Libraries Association; Medical Library Association.

Special awards, citations or publications.—NASA Exceptional Service Medal; Sustained Superior Performance Award, AEC.

BIOGRAPHICAL SKETCH

Name.—Kent Ashton Smith
Position.—Assistant Director for Administration, National Library of Medicine
Birthplace and date.—Boston, Mass., September 3, 1938
Education.—BA, Hobart College, 1960; MPA, Cornell University 1962.
Experience

Present—Assistant Director for Administration, National Library of Medicine; 1968–71—Executive Officer, Division of Research Resources; 1968—Acting Executive Officer, Division of Research Facilities and Resources; 1967–68—Assistant Executive Officer, Division of Research Facilities and Resources; 1962–65—Management Analyst, Office of the Secretary, Office of Management Policy.

Association memberships.—Sigma Phi Society; Society for Advancement of Management; American Society for Public Administration.

Mr. FLOOD. Is there anybody you would like to introduce?

Dr. CUMMINGS. Yes, sir. On my left is Mr. Kent Smith, the Assistant Director for Administration. I am also accompanied by Mr. Melvin Day, the Deputy Director and Dr. Ernest Allen, Associate Director for the extramural program.

Mr. FLOOD. I see you have a prepared statement. How do you want to handle that?

Dr. CUMMINGS. I would like your permission to read it and then answer any questions you and the committee may have.

Mr. FLOOD. Suppose you do.

OPENING STATEMENT

Dr. CUMMINGS. Mr. Chairman and members of the committee, when the National Library of Medicine was established 138 years ago in the Office of the Surgeon General of the Army, the medical literature consisted of a small collection of 30 books and journals. Since that time the volume of biomedical literature has expanded exponentially with the rapid strides in medical research, education, and practice. Today the NLM's total collection approaches 1.5 million items. U.S. medical journals alone have increased from 11 in 1936 to over 6,000 in 1974.

Mr. FLOOD. How long have you been there, Doctor?

Dr. CUMMINGS. This is the anniversary of my 10th year at the Library.

Mr. FLOOD. I want the record to show that.

Dr. CUMMINGS. Thank you. NLM faces the daily challenge of not only acquiring these books and journals, but also of organizing and efficiently disseminating this information to the health sciences community. All of our efforts have been directed toward achieving this overriding objective. We have developed a national biomedical communications network utilizing the latest technological advances which aids in the quality and timeliness of our information services.

BIBLIOGRAPHIC SERVICES

It was nearly 100 years ago that the National Library of Medicine first provided a guide to the medical literature, Index Medicus. In 1964 the NLM developed a computerized system for the production of Index Medicus known as MEDLARS. It incorporated an operational photocomposition system and for the first time provided individualized bibliographies or "demand searches" to health professionals upon request. The demand for such services grew rapidly as did the cost for formulation and review of such searches.

In 1971, a more timely and cost-efficient system was inaugurated known as MEDLINE—MEDLARS on-line. This on-line interactive bibliographic service allows the health scientist or physician to "converse" with the computer through a remote terminal to get more precisely what he needs, when he needs it. Searches now are completed in approximately 10 minutes rather than several weeks and cost approximately $7 rather than $60, the average cost of a previous MEDLARS search.

The response to MEDLINE in the biomedical community has been extremely gratifying. In fiscal year 1974, 250 institutions throughout the Nation will use the service, an increase of 50 percent over fiscal year 1973. The number of searches performed will total approximately 225,000—an increase of 40 percent over fiscal year 1973.

MEDLINE services are now being used by 225 institutions in 46 States and internationally by 8 foreign countries. In return for MEDLINE services foreign centers provide the equivalent of $250,000 in indexing of foreign language journal literature for input into the MEDLARS data base.

The widespread acceptance of MEDLINE and our projections of its continued rapid growth indicated a need to impose MEDLINE user charges to gain some control over the growth of the system and to provide a suitable funding alternative. In August 1973, charges were levied to offset the communications costs. These fees have made it possible to partially absorb toll charges for accessing the MEDLINE network and have equalized costs to users in regions remote from major urban areas.

We have continued to expand the on-line services through the implementation of new data bases. Three such services include: SDILINE, which is a complete file of those citations for the next month's INDEX *Medicus;* CATLINE, which provides access to catalog data on the monographic collection of the NLM; and SERLINE, which offers access to descriptive information on the 5,500 major biomedical serial titles and data identifying which libraries hold those titles.

Also, I would like to report on a new service planned for fiscal year 1975, namely, the addition of abstracts to the MEDLINE data base. The inclusion of abstracts will provide increased text searching capability and will enable health professionals to retrieve more specific medical information. In entering approximately 100,000 author abstracts in fiscal year 1975, NLM will have achieved another milestone in providing informative and ready access to the world's biomedical literature.

STATUS OF COPYRIGHT SUIT

Before turning to other specific programs of the NLM, I would like to inform the committee on the status of the copyright suit against the Government. The U.S. court of claims has ruled in favor of the Government in the alleged copyright infringement suit. An unfavorable decision would have required the NIH Library and NLM to pay for licenses and royalties for reproducing single copies of journal articles for use by health professionals, educators, and students. This would have greatly increased the operational costs of the NLM and other libraries throughout the country. While the decision of the court of claims may be appealed to the Supreme Court we are very encouraged by their decision. I would like, however, to continue to stress the need for new copyright legislation which hopefully would contain fair-use provisions allowing society to reap the benefits from the research it supports through grants and contracts.

Mr. PATTEN. From your Department for years we were supposed to get a little report on copyrights. You were here weren't you, Mr. Miller?

Mr. MILLER. I don't recall it.

Mr. PATTEN. Under education they promised. It had to be your Department. This is the only committee I am on. I remember in these hearings the last month or so I questioned about your recommendations for the change in the copyright rules. We have been waiting 3 or 4 years.

Dr. CUMMINGS. The only inquiry I am aware of was the one made by Mr. Robinson here last year. He expressed his interest and knowledge of this problem. I too am unware of the Departmental position dealing with this.

Mr. PATTEN. That came up in the previous hearings that you would try to get changes in the copyright laws so there could be a better dissemination of knowledge.

Mr. MILLER. I will check it.

Mr. FLOOD. Go ahead. Dr. Cummings.

TOXICOLOGY INFORMATION

Dr. CUMMINGS. Toxicology is a discipline that has acquired increasing importance because of current concerns about environmental pollution and its effects on health, about drugs and their potentially harmful effects, and about the potentially carcinogenic effects of chemical substances with which we come in contact. The National Library of Medicine's Toxicology Information program organizes data from scattered, diverse sources into a computerized storage and retrieval system. It also issues publications to satisfy needs for specialized toxicology information, and performs literature search services on request for the scientific community.

Fiscal year 1974 saw the end of the first year of operation of TOXLINE, the NLM's on-line toxicology information retrieval service. The system contains 300,000 records consisting of citations and abstracts from the published toxicology literature. The TOXLINE file includes data on pesticides, environmental toxins, pharmaceuticals, and hazardous household and industrial products. As of March 1974, over 80 organizations are paying users of the service, and 100 individuals have been trained in its use. In fiscal year 1975, we estimate that 50 additional organizations will be added to the list of users, and that annual usage will exceed 60,000 individual searches.

NATIONAL MEDICAL AUDIOVISUAL CENTER

At a time when there is much concern about the shortage of health care personnel and the large amounts of time and money required to train them, the National Library of Medicine is placing greater emphasis on the use of audiovisual media in health sciences education. Through its audiovisual component, the National Medical Audiovisual Center (NMAC) in Atlanta, Ga., the Library is working independently and in conjunction with the Office of Audiovisual Education Development of the Health Resources Administration, to strengthen biomedical audiovisual technology and make it more widely available for education.

The NMAC is developing a computerized data base of information on nonprint instructional materials relevant to professional education in medicine and the allied health sciences. The program already has evaluated, cataloged, and indexed approximately 2,000 titles to be included in a clearinghouse of such materials, and has entered a portion of the titles into an NLM computer for testing. Information on the organization and management of biomedical communications programs in 55 schools of the health professions also is being entered into the computer. This file, to be updated periodically at NMAC, will serve as an information resource for providing advisory services to other schools of the health sciences.

The NMAC cooperates closely with professional organizations to evaluate instructional media for quality and appropriateness of content. In addition, agreements with groups, such as the American Association of Medical Schools and the American Association of Dental Schools, provide NMAC with continuing feedback on the actual use made of these instructional materials.

NMAC produces or acquires for distribution instructional media not available from professional or commercial sources. In fiscal year 1974, approximately 65,000 requests for film loans of audiovisuals were filled from the NMAC collection, and approximately 2,500 videotapes were duplicated for the use of health scientists.

By tapping the potential of audiovisual technology, the Library hopes to make a contribution toward increasing the Nation's supply of health manpower and to meet more effectively the growing need for information in nonprint formats.

BIOMEDICAL COMMUNICATIONS RESEARCH AND DEVELOPMENT

In 1968, Joint Resolution 193 was signed into law creating the Lister Hill National Center for Biomedical Communications to serve as the focal point within the Department of Health, Education, and Welfare for the development and coordination of communication networks and systems to improve health education, medical research, and the delivery of health services. While many advances in biomedical communications technology have already resulted from this program, full potential will not be realized until the Lister Hill Building is constructed. The architectural and engineering final drawings will be completed by the end of calendar year 1974. I would like to describe briefly some of the experimental and operational systems which the Center is currently supporting.

SATELLITE NETWORKS

Probably there never will be a satisfactory substitute for face-to-face communication between doctor and patient or instructor and student. Where that kind of interaction simply is not possible, however, modern telecommunications technology can go a long way toward filling the gaps. In Alaska, for example, residents are widely dispersed in geographically remote regions, health professionals are few and far between, and conventional radio communications are unreliable.

Faced with these problems, the Lister Hill Center set out over 2½ years ago to demonstrate the potential of satellite communications for improving health care and education. We developed an experimental voice network linking over 20 Alaskan Native villages with Indian Health Service hospitals and major medical centers.

The network, which employs a NASA applications technology satellite (ATS–1), has clearly demonstrated the benefits of improved voice communications for the health care of widely dispersed populations.

In fiscal year 1975, the Center will expand the network with an experimental communications link to the Indian Health Service's information service in Arizona. This will permit the village clinics to obtain up-to-date medical records on patients to assist health professionals in their treatment.

The next phase of satellite experiments will start in June when NASA will launch an applications technology satellite–F (ATS–F). Experiments using this satellite will evaluate the effectiveness of live television consultation between physicians at the Indian Health Service hospitals and health aides at several remote clinics in Alaska. In addition, with LHC support, the University of Washington will use the ATS–F satellite to provide instruction for first-year medical students at the University of Alaska and for students taking their preceptorship under physicians in selected isolated rural areas of Washington State. The purpose of this project is to evaluate the effectiveness of direct satellite television broadcasts for medical education.

COMPUTER-ASSISTED INSTRUCTION (CAI)

The Lister Hill Center is operating a national network to promote the sharing of programed educational resources among medical institutions. University medical centers with good computer-assisted instructional programs are connected through to the NLM national communications network. The use of their computers and programs are then offered to other institutions which integrate the programs into their own curricula, evaluate them, and produce additional units of instruction. In fiscal year 1974, 80 hospitals, medical schools, and dental schools were using the CAI network. It provided an average of 12,000 student instruction hours per month.

Beginning in February 1974, the Lister Hill Center required users to pay a share of the communications costs of the network. In fiscal year 1975, the charge will be increased, but the center will attempt to find ways to make CAI available at a lower cost than is possible with the present network.

CABLE TV

During fiscal year 1974, the LHC introduced the concept of "cable television for health" to the elderly population of a public housing unit in New York City. The center decided to work with a geriatric population because the elderly suffer more illness for longer periods of time than any other age group. They also account for a disproportionate share of the Nation's expenditures for health. Although comprising less than 10 percent of the population, the aged account for 27 percent of our total health bill.

The aim of the project is to use cable TV creatively to reduce the social isolation of the residents and to disseminate health information to them. Operating on the premise that television is probably the most important communications medium in the lives of older people, the project will use a cable television system with interactive capabilities to establish two-way communication.

As these projects prove to be feasible, useful, and cost effective, the center attempts to make them fully operational with a gradual withdrawal of NLM funding. Thus, the Lister Hill Center serves as a test bed for the application of advanced communications technology to assist in the solution of our medical information problems.

MEDICAL LIBRARY ASSISTANCE

The programs of medical library assistance form one vital component of the biomedical communications network. The regional medical library (RML) system is funded by extramural program funds which provide assistance for delivery of documents and for planning an efficient and coordinated system of medical information services. The most effective method of deploying the technical achievements and advances of NLM and of implementing national health communications policies is through these regional centers. The grant programs aid the service-oriented partnership of NLM and RML's by: (1) regional grants to develop and test new network activities; (2) resource grants to develop community library and information services; and (3) research grants to investigate and develop more effective procedures in biomedical librarianship, the flow of health information and health communication tools.

Still another grant program provides assistance in the training of health science information specialists in the application of computer technology to medical education and practice. People soundly grounded in both medical science and computer technology are needed to apply new technologies toward the development of innovative approaches to medical education and health care delivery. We believe that the cooperative application of these two disciplines can greatly improve systems development for the health of our Nation.

In conclusion, to fulfill our mission the fiscal year 1975 budget request for the National Library of Medicine is $27,738,000. This is $1.5 million more than the fiscal year 1974 budget authority but $2 million less than the amount available for obligation this year.

I will be very pleased to answer any questions the committee may have.

1975 REQUEST

Mr. Flood. Your budget for 1975 is $27,738,000, as you said, an increase of $1.4 million over the 1974 adjusted appropriation. Is that right?

Dr. Cummings. Right.

Mr. Flood. What program areas in the Library of Medicine will benefit most from this increase of $1.4 million?

Dr. Cummings. We have been forced, Mr. Chairman, to set the priorities favoring the maintenance of our ongoing direct service capabilities. So in essence the new funds will primarily be used for the nonconventional as well as the traditional library services we provide the Nation. None of these funds unfortunately will be available for the extramural program.

REIMBURSABLE SERVICES AND USER CHARGES

Mr. Flood. In addition to the money appropriated annually by Congress, you are also reimbursed for some of your services. Is that right?

Dr. Cummings. Yes, sir.

Mr. Flood. How much will you collect in 1975 for these reimbursable activities?

Dr. Cummings. I don't know that I can give you the estimate offhand but I can provide it for the record.

Mr. Flood. I wish you would.

[The information follows:]

NLM will expend and recover in addition to its annual appropriation approximately $1.5 million for services and materials utilized in performing library and audiovisual projects for the benefit of other Government agencies A schedule of anticipated reimbursable income to be received in fiscal year 1975 by Government agency is as follows:

NATIONAL LIBRARY OF MEDICINE—REIMBURSEMENT INCOME

[In thousands of dollars]

Activity, agency and types of services rendered	Actual fiscal year 1973	Estimated fiscal year 1974	Estimated fiscal year 1975
Library operations:			
Agency for International Development: Library servces	60	65	75
National Institute of Environmental Health Services: Library services	5	10	
National Medical Audiovisual Center:			
Pan Am Health Organization: A/V services	8	15	40
DHEW, HSMHA: A/V services	40	125	175
Environmental Protection Agency: A/V services	4	10	35
Veterans' Administration: A/V services		10	35
NIH: A/V services		15	20
DHEW, HRA, BHRD: A/V services	820	870	1,000
Department of Defense: A/V services		20	60
Other: A/V services		20	35
Office of Computer and Communications Systems: GSA: Computer services	26	25	25
Total, NLM	963	1,200	1,500

In addition to its reimbursable activity, the NLM has instituted a user charge policy for its computerized search services. The imposing of user charges permits NLM to apply its appropriated resources to the maintenance of the communications network while having the users pay directly to the contractor, the cost of accessing the system. It is anticipated that NLM users will be billed by the contractor approximately $658,000 in fiscal year 1975.

NLM does receive revenue for library services performed at Bethesda, Md. However, these receipts are deposited in the U.S. Treasury. NLM anticipates approximately $20,000 for these services in fiscal year 1975.

Mr. Flood. Are you making any attempt to increase the level of these user charges thus putting the program more on a self-sustaining basis?

Dr. Cummings. We are doing this gradually, and I should say more as a management control than for recapturing funds from the user community. We have implemented user charges to gain management control and prevent any frivolous use of the system.

To answer your question, we have no intention, Mr. Chairman, of trying to run our National Library of Medicine on a totally reimbursable cost basis.

Mr. Flood. Suppose you give us a couple of examples of services you perform at the library for which there is what you call a user charge.

Dr. Cummings. All of the computer search services that we provide in behalf of the Nation's physicians, scientists and educators have a user charge. The charge is geared to recapture the communications cost involved in accessing the system, but we do not charge for the intellectual work the library has done to build the data base because this is work we have done for over a century and is a prime obligation of the library.

Mr. Flood. These current amounts being collected in user charges, is that the maximum amount you think will be collected?

Dr. Cummings. No, sir. I see now I can give you a full answer to your question. Mr. Smith shows me that our user charge estimate for fiscal year 1975 is $658,000. That is a sizeable increase over this year and I would expect this trend to continue.

LISTER HILL CENTER FACILITY

Mr. Flood. Last year you told us about the Lister Hill Center. Last year you told us the architects were going to have the design for the Lister Hill Center completed by February 1974. A few minutes ago in your opening statement you said it would be the end of the calendar year 1974. Why the delay?

Dr. Cummings. You are absolutely correct. There has been a slippage on the part of the architectural firm completing the engineering and architectural design of the building. But we are now assured from our own examination of the state of their work that they will complete the total planning and design by December of this year.

Mr. Flood. That is going to be over 2 full years simply to complete the design for the project. Is that right?

Dr. Cummings. Mr. Chairman, the major——

Mr. Flood. It is over 2 years by the time they finish it.

Dr. Cummings. It is over 2 years, but the major delay took place by the impoundment of our planning moneys in the Office of Management and Budget. There was a 2-year delay when those funds were not made available. So the delay really is a total of 4 years.

Mr. Flood. We just hope you don't come up here next year with a new completion date.

Dr. Cummings. I am quite confident in saying today that we will be prepared to go out for bids in the next calendar year.

Mr. Smith. Will the chairman yield?

Mr. Flood. Yes.

Mr. Smith. Is there money in the budget so you can go out for bids?

Dr. Cummings. There is no money in the budget for construction of this facility.

Mr. Smith. Then you couldn't go out in the next calendar year could you?

Dr. Cummings. We could not without your authority and appropriations. I indicated we would be prepared to do so.

Mr. Miller. He says, as I understand the conversation, that the architects won't be ready until December which is halfway through the fiscal year. I think normally we don't put construction funds in the budget when we are that far along in the fiscal year.

Mr. Flood. That is why I indicated I hope you don't come back here next year with a new completion date.

CABLE TV

In your opening statement you listed several projects that are underway at the Lister Hill Center. One of these projects involves cable television as a means of bringing information to the elderly at a New York housing project.

Tell us more about that. Will these elderly be able to communicate their problems directly to the medical center and will the medical center be able to prescribe treatment over the TV?

Dr. Cummings. First let me say, Mr. Chairman, that we are opportunists in the library, and I want to be sure the committee understands we did not pay for the laying of cable between Mount Sinai Medical Center and this housing project. We learned this new project would have cable TV and we approached the medical center and the community to see if we might perform a service.

To answer your question regarding how it will be used, at the outset there will be two-way voice communication and one-way television communication. That is to say that mobile cameras will be available in the settlement house through which the patient could be displayed to the physicians at Mount Sinai and through which there can be a patient-physician discussion.

The second part of the development will make it possible for two-way interactive television.

The programs that are being written for the settlement house are those that are ordinarily considered to be health education, such as how to take care of your diabetes if you have it. There will be regularly scheduled health educational programs, and there will be clinics held by conversations between doctors and the elderly where one might say there is a sick call. Patients will announce to the doctor what symptoms they have, what has happened to them since their last conversation.

Mr. Flood. Do you have any other uses in mind for the cable TV?

Dr. Cummings. No, sir. We hope that we can get a sufficient evaluation to this one setting to then allow us to design other experiments if this proves successful.

Mr. Flood. You mentioned also in your statement about the project for the elderly, if it proved feasible—you are talking about useful and being cost effective. You said you intend to make them fully operational and that would be done by gradual withdrawal of the National Library of Medicine doing any funding at all.

Dr. Cummings. That is right.

Mr. Flood. How will the cable TV project for the elderly work? Will it pay for itself or where is the money going to come from?

Dr. Cummings. There are discussions taking place with various interested civilian groups, including labor groups among others, who might very well wish to assume the responsibility for maintenance of this operation. If we can demonstrate it is not a high cost operation, I believe the community will support it.

Mr. FLOOD. The community?

Dr. CUMMINGS. Yes, the interested community.

Mr. FLOOD. You don't mean the municipality?

Dr. CUMMINGS. No.

Mr. FLOOD. You are not using the term in that sense?

Dr. CUMMINGS. No. I mean interested private groups.

LISTER HILL CENTER

Mr. FLOOD. We understand reports come in about the Lister Hill Center that are pretty good, excellent. Suppose you place in the record a report on the progress of the projects now at the Lister Hill Center as well as those projects which you have in the planning stage and development stage to make this record on the Center look as we think it should look over here.

Dr. CUMMINGS. We are very proud of the center and will be pleased to provide such a report.

[The information follows:]

NATIONAL LIBRARY OF MEDICINE, LISTER HILL CENTER PROGRESS AND PLANS

The enclosed collections of materials briefly highlight the projects the Lister Hill Center is currently engaged in supporting.

A comprehensive report will be furnished to the committee outlining the center's plans for future program emphasis and development.

ALASKA SATELLITE PROJECT—DIAGNOSIS BY SATELLITE: DOCTORS HAIL ALASKA TEST

In March in the remote village of Allakaket with a population of 125, a medical aide tried in vain to contact the PHS in Tanana, Alaska. An 11-year-old girl, Sally Sam, was seriously ill. The aide finally reached an ATS ground station. He was put through, via the ATS radio to physician David Duncan in Tanana. Duncan's diagnosis was acute appendicitis. Within 15 minutes of the call, the girl was picked up by an aircraft and taken to a hospital.

Similar stories can be told of Lincoln Mark, a native of Huslia, who had been injured in a snowmobile crash; of another acute appendicitis case in Anaktuvuk Pass, and of a hemorrhaging woman in labor in Chalkyitsik.

[From the Science News, July 8, 1972]

RESEARCHERS HELP PROVE WORTH OF SATELLITE SYSTEM

An experimental satellite communication system has dramatically improved the delivery of health care in 14 remote Alaskan villages and should be expanded to other isolated areas in the State, Stanford researchers have reported.

One portion of the research was a film, "Satellite House Call," made by Judy Irving as her master's project in Department of Communication. Assisting her were John Nutt, graduate student in film, and his wife, Ann.

The satellite service enables native health aides—who have at most only 16 weeks of training, yet provide all the primary medical care in their communities—to obtain needed daily consultation from doctors at an Alaskan field hospital.

[From the Anchorage Daily Times, Oct. 8, 1971]

TWO ARE SAVED BY ALERT USE OF SATELLITE

WASHINGTON, D.C.—The lives of two native women were saved by the alert use of the communications satellite system serving remote villages in Alaska, reports Senator Mike Gravel, D-Alaska.

[From the Journal of the American Medical Association, Dec. 17, 1973]

CABLE TV PROJECT—CABLE TV LINKS HOSPITAL, APARTMENTS

HEW's National Library of Medicine (the Lister Hill National Center for Biomedical Communications) is coordinating the planning for a two-way cable television link between Mount Sinai School of Medicine, New York City, and a 248-apartment public housing high-rise (Gaylord White House) in East Harlem. Plans tentatively call for:

Cable television in each apartment for the 339 tenants, whose median age is 69.

Two-way communication, allowing tenants to ask questions and participate in discussions of nutrition, exercise, household safety, chronic diseases, and other health-related topics of interest to the elderly.

Monitoring of the tenants (without their leaving home) by Mount Sinai medical people using astronaut-type remote sensing devices for blood pressure, heartbeat, body temperature, and other signs.

Studies of how to communicate health information effectively to the elderly via this medium, including pre-testing programs with small groups of tenants before cablecasting to the entire tenant population.

[From the Medical World News, Nov. 30, 1973]

HEALTH CARE FOR ELDERLY VIA TV

Watching television may become an important way for older people to take care of their health. A new Federal study will explore the use of a two-way cable TV hookup linking New York's Mount Sinai Medical Center with 248 apartments in an East Harlem high-rise public housing building, where the median age of the 339 tenants is 69. With a $200,000 grant from HEW, Mount Sinai will activate an unused TV channel for the exclusive use of these residents and the hospital. Special programs will be produced on such subjects as diabetes; preparing low-cost, high-nutrition diets; household safety; and exercises for the elderly. With two-way communication, tenants can also ask and answer questions. And, utilizing equipment developed by NASA for astronauts, personnel at the medical center will be able to monitor and record heartbeat, temperature, blood pressure, and other body signs of patients who are in their own apartments.

[From the Parade magazine, May 13, 1973]

COMPUTER-ASSISTED INSTRUCTION—MEDICAL STUDENTS WHO NEVER GO TO CLASS

Ohio State's project—supported by a Federal grant of more than $1 million—is called independent study program (ISP) and has far-reaching implications toward producing more and better doctors to fill the chronic shortage. In ISP a medical student is, to a great extent, put on his own responsibility. Faculty members, of course, tell the students what to study—which books to read, and what slides and tapes to use on the audiovisual teaching machines. But from there on it's mostly up to the student.

[From the New York Times, Apr. 29, 1973]

INTERACTIVE TV NETWORK—CLOSED TV NETWORK LINKS FOUR HOSPITALS

HANOVER, N.H., April 28.—An interstate medical communications system was dedicated on Thursday iln Hanover and Claremont, N.H., and Burlington and Berlin, Vt.

The two-way, closed circuit television network links the Dartmouth Medical School with the University of Vermont Medical Center in Burlington, the Claremont General Hospital and the Central Vermont Medical Center in Berlin.

The network was developed by the Dartmouth Medical School from an original television link connecting the Dartmouth-Mary Hitchcock Hospital in Hanover with Claremont General Hospital.

The system will enable doctors and nurses in any of the four hospitals to observe doctor-patient sessions, discuss the case on the spot, or exchange information among themselves. Other hospital employees who may use the system, include medical and speech therapists, nursing home staff members, and technologists.

The expansion of the television link was made experimentally with financial help from the Lister Hill National Center for Biomedical Communications.

[From the Valley News, Apr. 27, 1973]

MEDICAL CENTER DEDICATES INTERACTIVE TELEVISION NET

HANOVER.—About 100 persons were given some firsthand examples of how closed circuit television can benefit the medical and allied health professions Thursday during the dedication of the new Interactive Television Network.

[From the Sun, Oct. 8, 1971]

ALASKA SATELLITE PROJECT—SATELLITE HELPS SAVE 2 LIVES

WASHINGTON.—Two women in remote native villages of Alaska were saved from possible death last week by medical instructions relayed by satellite.

Space agency officials hailed the unplanned emergency services as a striking demonstration of the value of static-free satellite communications in parts of the world where atmospheric disturbances frequently interfere with or block the reception of radio signals.

[From the Biomedical News, March 1972]

SATELLITE LINKS REMOTE ALASKANS WITH DOCTORS

Medical traffic is so heavy that the satellite is turned on 7 days a week for 6 or 7 hours a day. This year, a full time doctor was stationed in Anchorage in connection with the program.

In two life-saving instances, a doctor in Tanana instructed medical aides in other villages on patient care for premature bleeding in pregnancy and for a suspected rupturing appendix. Later, both patients were successfully transported to other locales for definitive treatment.

TOXICOLOGY INFORMATION PROGRAM

Mr. FLOOD. You mentioned in your opening statement a toxicology information program and say there are some 80 organizations actually paying users of the program.

Dr. CUMMINGS. Yes, sir.

Mr. FLOOD. Who are some of the users? What kind of information do they seek?

Dr. CUMMINGS. Users comprise an interesting mix of professional groups concerned with drugs, chemicals, and toxic effects of certain materials. The pharmaceutical industries are deeply interested in this kind of information and they are subscribers. The universities that have programs in pharmacology and toxicology are also users. But importantly, Mr. Chairman, the Federal agencies of our Government, the Food and Drug Administration, the military services, the Veterans' Administration among others are also users of the system.

Mr. FLOOD. Do you see any development or increase in the number of users of the system? How many would there be and what kind of users would there be?

Dr. CUMMINGS. We are pleased, as I have reported, that we now have 80 institutional subscribers and the system is only 1 year old. I think it will double in the next 2 years, and I think as the data base is enriched with more information, it may very well become one of the most important computer data bases in our Nation.

I would add that Dr. Rall is the coordinator for DHEW of all the agencies that have interests in pharmacology and toxicology information, and he and his committee are used by us as professional advisers and technical advisers about the quality and characteristics of the data base that we are building. This is very helpful.

NATIONAL MEDICAL AUDIOVISUAL CENTER

Mr. FLOOD. Doctor, in the last 2 weeks we have heard a great deal of testimony here from various Institutes about the need for a patient education program. That phrase runs all through the testimony here.

Can the National Medical Audiovisual Center play a role in meeting the need everybody says is there? In what way can it help the health maintenance organization to meet its commitments to provide patient education and so on, health education courses to membership of an HMO for instance?

Dr. CUMMINGS. The National Medical Audiovisual Center in my judgment could be of assistance in developing this kind of program material. In fact, in past years it did contribute considerably to such things as spot television programs on measles immunization, polio vaccination, how-to-do-its that related to health. But because of our constraints on staff and budget we have been forced to put that at a lower priority level and to address most of our energies and talent to the field of health professional education. But the resource is competent to engage in this kind of work if it were elaborated.

CABLE TV

Mr. FLOOD. You certainly know the horizon for what you are talking about for the transmission on cable TV's. It can be a can of worms.

Dr. CUMMINGS. I think the key to success is quality of programing, and it would be a bunch of worms if we put garbage on the air. I can assure you that is not our intent and we are very careful in evaluation of materials before they are disseminated.

Mr. FLOOD. Big Brother is going to be watching this one.

Dr. CUMMINGS. I am sure that will happen and I am sure Big Brother should.

MEDLINE SERVICES

Mr. FLOOD. Mr. Robinson.

Mr. ROBINSON. Thank you, Mr. Chairman.

Doctor, you mentioned the fact that the MEDLINE services are now being used by 225 institutions in 46 States. With regard to their connection with the MEDLINE network is there a basic expense that must be borne by the Institute in order to get "on line" and is that borne by the Institution itself or did you subsidize it?

Dr. CUMMINGS. Your question is most appropriate, because there is a basic expense that an institution bears when it joins the network. The first commitment it must make is to share the terminal resource with a community that surrounds the institution. The institution must pay for is own terminal, its little hardware, and then pay for the communications cost, say, to reach from Charlottesville to Bethesda. So it is a shared system.

What we pay for is the generation of the system, its design and implementation, and the maintenance of the information bank which everyone reaches into.

Mr. ROBINSON. Is the hardware that is necessary specific to MEDLINE or does it have any other uses as well?

Dr. CUMMINGS. Fortunately it has multipurpose utility, so that a terminal that can reach our data bank can also be used to search other data banks. Fortunately also, in my view, Mr. Robinson, the cost of these terminals has come down considerably. One can purchase a terminal for about $3,000 or $4,000, and they are quite sturdy. They can also be leased for several hundred dollars a month. So, it puts it within the reach, for example, of a community hospital, which is a group we are very much interested in.

I might add even the Director of NIH is now using a terminal and is one of our users, and we are very pleased he is on line.

Mr. Robinson. You commented in our colloquy of last year with regard to copyrights, Doctor. I wonder if the experience in taking this matter to court has changed your viewpoint any with regard to the statement which is in the record as of that point in time?

Dr. Cummings. No, it has not. My view remains the same now as it was at the time we discussed this earlier. I am just a little more confident now that our view has legal merit as well as other merit.

Mr. Rorinson. Looking a little further into our colloquy of last year, I notice that you mentioned that the cost of a given inquiry with regard to MEDLINE at that time, the access charge would run between $2 and $2.50 whereas your statement mentioned what I presume is a similar inquiry today would be $7. Is that correct?

Dr. Cummings. The total costs of providing a MEDLINE service is between $7 and $7.50 depending on the distance and other factors. Half of that cost roughly is borne by the institutional user.

Mr. Robinson. So the total cost is not then borne by the Institution?

Dr. Cummings. The Institution bears about half of the cost of the total search.

Mr. Robinson. I certainly want to congratulate you on the fact that the cost of such inquiries has come down from what you stated, $60 to $7 now.

Dr. Cummings. Thank you.

Dr. Robinson. On page 246 of your justification which has to do with regional medical libraries, you mentioned the probable or potential involvement of such libraries in the work of the newly established or to be established PSRO's. These, of course, are controversial among our doctors State by State, and I wonder to what extent it is proposed that these RML's would be involved in the work with PRO's?

Dr. Cummings. I am pleased to deal with that question.

One of the blessings and one of the great joys of working in the National Library of Medicine is that it serves an entire health community regardless of attitudes or other factors. We serve the association of physicians, the pharmaceutical industry, the academic community, and over the century of service we have their trust and respect.

This program that is described here merely indicates that if there will be area health education centers, PSRO's, State or units within a State, that we are committed to share medical information with them as we do with others. We are not involved in PSRO's beyond a commitment to give physician and the managers of these systems information that they need. It will be medical information from the literature, not patient records or insurance records.

Mr. Robinson. That answers the next question I had in mind as to whether or not you intended to build a data bank with regard to patient records and costs per service, which I think would be inappropriate.

Dr. Cummings. Yes, it would be inappropriate.

Mr. Robinson. I am glad to hear such is the case.

You mentioned your interest in cable TV and what can be done in that regard. I wonder if a possible involvement and use of public TV has also been examined because it seems to me this would be a very proper area for the dissemination of information to the elderly, in particular, because of their inclination to watch so much TV and public TV of course is coming up in viewer popularity all the time.

Dr. Cummings. I would have to be careful to distinguish my personal view from a more official view in response to this question.

One of the things we are trying to do is to avoid a competitive arrangement with the existing commercial sector that manages television.

I personally believe this kind of health programing would be useful, but I don't think that the National Library of Medicine should be leaning on the industry to do this, and that is why we have chosen these small mini-networks of cable television that are looking for new kinds of programs and are receptive to our proposition.

Mr. Robinson. I congratulate you on an excellent statement, doctor. Thank you very much.

NEED FOR NEW LISTER HILL FACILITIES

Mr. Flood. Mr. Smith.

Mr. Smith. You said in your statement the full potential of biomedical education technology will not be realized until the Lister Hill building is constructed. I believe later in the colloquy you said it had been delayed by 2 years by impoundments of funds. It sort of disturbs me we are not getting the potential out of a big investment because we didn't have the building to operate from.

How much is this building going to cost?

Dr. Cummings. The total estimate for the completion of the building is $19.8 million.

Mr. Smith. That is estimated on present prices; correct?

Dr. Cummings. That is estimated on the basis of having an appropriation that might allow us to have the building in 2 or 3 years.

Mr. Smith. How much additional is it estimated to cost for each year of delay?

Dr. Cummings. Twelve percent per annum. The original estimate we gave this committee when you provided planning funds would have called for construction expenditure of $12 million.

Mr. Smith. And so the plans will be ready at the end of this calendar year, is that right?

Dr. Cummings. That is correct.

Mr. Smith. And so if money were available in this budget which is not in the budget, you could start early in the next calendar year?

Dr. Cummings. I believe that is technically correct. I better turn to Mr. Smith who is managing this project and see if he agrees with this estimate.

Mr. K. A. Smith. That is absolutely correct. If we had the money we could go out for bids, and early in the calendar year be able to actually award a construction contract.

Mr. Smith. How much space are we talking about?

Dr. CUMMINGS. A little more than 200,000 square feet.

Mr. SMITH. This space apparently is critically needed.

Dr. CUMMINGS. The space is needed, but more importantly the facility is a special purpose facility that you just can't lease or find in the community. It is like the NIH intramural program and the clinical center with its own laboratories. This will be special purpose engineering and communications laboratory space among others.

Mr. SMITH. This space is needed before you can, in the words you used in your statement, secure the full potential from the biomedical communications technology now available?

Dr. CUMMINGS. I believe that to be true.

Mr. SMITH. What will the building look like?

Dr. CUMMINGS. It will be a 10-story tower to be located at the site adjoining the present National Library of Medicine on the campus at NIH.

Mr. SMITH. When you say site adjoining, could one walk inside from one to the other?

Dr. CUMMINGS. They will be connected aboveground and underground with the present facility. The facility will accommodate the computer resources that we now have in the Library as well as the engineering and communication resources that we are looking for.

Mr. SMITH. That is all, Mr. Chairman.

USERS OF TOXLINE AND MEDLINE

Mr. CONTE. Have you collected any information on who uses TOXLINE and MEDLINE services for what purpose?

Dr. CUMMINGS. NLM has analyzed data on the use of MEDLINE. During the period July 1973 to February 1974 about 24,000 search requests in the Mid-Atlantic Region, comprising Maryland, West Virginia, Virginia, North Carolina, and the District of Columbia, were analyzed. The distribution among users was as follows:

	Percent
Research	43
Patient care (physicians only)	27.5
Allied health personnel	5.5
Students	16
Others	8

Because of the large number of Federal users in the Washington area, it is possible that the number of research users in that area may be unusually high.

An independent study for the period September 1, 1972, through March 31, 1973, at the University of Virginia Medical School at Charlottesville was recently published in the Bulletin of the Medical Library Association in January 1974. These results are as follows:

	Percent
Medical school faculty	26
University of Virginia hospital physicians	20
Physicians outside of university hospital	19
Graduate students in health fields	12
Medical students	11
Nursing school faculty and students	5
Miscellaneous	7

The TOXLINE data base has just recently been transferred to the NLM computer. User group analysis will be made in the near future.

Mr. Conte. Have any former MEDLINE users been unable to continue because of service charges?

Dr. Cummings. The implementation of charges has not resulted in any discontinuance of MEDLINE Centers. Only two organizations, both Federal institutions, have terminated their agreements. These have been for other reasons. There is no specific information as to whether any individuals have not been able to use the services because of fees.

LISTER HILL CENTER

Mr. Conte. Are staff of the Lister Hill Center engaged in any kind of joint planning with the Health Services Administration to explore ways of providing information services to delivery organizations, especially in remote areas?

Dr. Cummings. The Lister Hill Center is working with the Indian Health Service of the Health Services Administration in planning and carrying out the Alaska health experiment with the ATS–F satellite. We expect to work with IHS and other health agencies in coordinating the planning of services requiring extensive communications systems.

MEDICAL LIBRARY RESOURCES PROGRAM

Mr. Conte. Will help be available through the medical library resources program to new kinds of delivery organizations, such as HMO's, or is it limited to medical schools and their libraries?

Dr. Cummings. One of the primary purposes of the resource grant program is to facilitate and improve the provision of more effective information for the physicians and other health workers in the delivery of health care. The resources provided for this purpose are currently located in educational institutions and hospitals with health libraries. With additional resources an active effort could be made to extend this type of support to additional hospitals and educational institutions which could support certain informational needs of HMO's and similar health-centered institutions.

MEDLINE

Mr. Conte. Is MEDLINE still limited to research literature, or has it been expanded to cover the literature on health services?

Dr. Cummings. The MEDLINE data base has had extensive coverage of literature in all the major fields of medicine and related sciences. This includes literature in all fields of health services. Until February 1974, this coverage was limited to the top 1,000 of approximately 2,300 journals covered by Index Medicus and contained a higher percentage of research literature. Since February 1974, the MEDLINE data base has been regenerated and expanded. It now includes all the literature appearing in Index Medicus.

FOREIGN LANGUAGE PUBLICATIONS

Mr. Conte. Does the Library have any program to translate and make available the mainland Chinese medical research literature?

Dr. Cummings. The Library does not maintain translation services for foreign language publications. Through its extramural programs it has supported the translation of publications in foreign languages. Should there be an active need to provide such information, it would be possible to develop translation programs for mainland Chinese medical research literature. The newest Chinese medical journals currently received by NLM contain either full English language articles or English language abstracts of the clinical articles.

INTERACTIVE TV PROJECT

Mr. CONTE. You're planning to change the interacitve TV project from a research one to an ongoing, self-supporting system. Are you going to provide technical assistance to potential users?

Dr. CUMMINGS. No, or at least no more than to any other NLM user. The Lister Hill Center has transferred responsibility for providing such services to the staff of Interact, the New Hampshire/Vermont medical interactive television network. This is an important part of their program to become self-sustaining, finding prospective users and showing them how to use the system. This assistance is better given by the Dartmouth network peronnel.

Mr. CONTE. Are there potential users elsewhere in New England ready to install the system now?

Dr. CUMMINS. The White River Junction Veterans Administration Hospital is now requesting proposals for the necessary transmission links to connect to the network at Dartmouth by the first quarter of fiscal year 1975. The USAF AFB at Platsburgh, N.Y., expects to start work on a link across Lake Champlain to the University of Vermont in Burlington in the first quarter of fiscal year 1975, for the purpose of providing consultation from UVM physicians to the base hospital.

Other civilian institutions who have expressed interest in becoming affiliated with the network are: St. Johnsbury Hospital, St. Johnsbury, Vt.; University of New Hampshire, Durham, N.H.; Maine Medical Center, Portland, Maine; Elliott Hospital, Manchester, N.H.; Keene, N.H., Hospital; New London Hospital, New London, N.H.; Bennington Hospital, Bennington, Vt.; Newport General Hospital, Newport, N.H.; Littleton Hospital, Littleton, N.H.; and Berlin Hospital, Berlin, N.H.

EXTRAMURAL PROGRAM

Mr. OBEY. You said that none of the new funds requested for 1975 will be available for the extramural programs, and you used the word "unfortunately." Why do you deem this unfortunate?

Dr. CUMMINGS. Although small in size, the extramural program has moved far toward developing a national library network aimed at providing health practitioners, regardless of physical location, with equal access to information necessary for the provision of better health care. Fund limitations now would curb the momentum that has built up and jeopardize the confidence in the network that has been slowly but steadily growing for 8 years. New educational technologies exist to help us learn better and faster. We need to integrate these new methodologies into libraries to create a total learning resource. We need to capitalize on the foundations laid over these 8 years.

Mr. OBEY. Given the level requested for the extramural program, how can the library needs of hospitals, medical centers, and allied health institutions be met, particularly with rising costs in the acquisition of sophisticated technology?

Dr. Cummings. It would not be my recommendation to attempt to meet all this Nation's health information needs solely through the fiscal assistance provided by our extramural program. This would be an impossible task. Rather, we seek with these programs to solidify a system of national coordination. Slow but continuing progress toward this objective has been made, and it is our hope that this progress will continue.

Libraries exist to provide information services. A great deal needs to be done to encourage more active delivery of these services to the health practitioner wherever he may be. It is only through the vigorous support of new and innovative projects that this can be accomplished. However, more than 75 percent of the extramural projected fiscal year 1975 budget is committed to the continuation of ongoing projects. Libraries are experiencing not only diminishing fiscal resources, but spiraling costs for information materials and equipment, in spite of accelerating information demands. A continuation of this condition could inevitably lead to failure of our national health information efforts.

REDUCTION IN LIBRARY GRANTS

Mr. Obey. Concerning the lower figure allocated in the budget to the medical library resource grant program which provides stimulus and aid to local community hospital libraries throughout the country, what would you consider to be an optimum level of funding for this type of resource program?

Dr. Cummings. My best estimate of an optimum level of fiscal year 1975 funding for the medical library resource grant program, is $2,500,000, a figure somewhat below our fiscal year 1974 level of support. The primary purpose of this funding is to build up the community hospital libraries throughout the country and thus strengthen the regional medical library system. The community hospital libraries provide the first point of access to information services for the great majority of healthworkers. These libraries are basic building blocks of the network. In 1969, only 1,700 of the estimated 7,600 hospitals in the United States had library resources greater than 500 books and 25 journal titles.

Mr. Obey. Will not the proposed budget cut in the resource grant program, and in the regional medical libraries slow down the development of this network, at the very time it is most needed by physicians and allied health personnel and their continuing education programs and possible new relicensure requirements?

Dr. Cummings. The proposed budget cut in resource grants and in the regional libraries does come at the very time when expanded services of medical libraries are needed. There are many new programs for physicians and allied health personnel which will create increased demands for information. These include area health education centers, PSRO's, HMO's, as well as continuing education requirements. The information needs thus generated can only be met efficiently through a cooperative network. It is the purpose of the RML network to provide rapid, consistent, and reliable information service to health care practitioners at the community level where they need it most. We are supporting innovative programs that bring information even to the bedside of the patient. These kinds of new outreach information services contribute directly to improving the quality of health care that is needed.

TRAINING GRANTS

Mr. Obey. Dr. Cummings, please comment on the considerable cut in training funds in the 1975 budget. It seems to me that with all the new approaches including the computer technology, MEDLINE, and other innovations in medical libraries, that the hospital librarian, the physician, and the healthworker will require additional specified training. What do you consider would be the optimum budget for library training to meet these needs?

Dr. Cummings. I do not advocate further training of personnel at this time for traditional library practices. I do believe, however, that special training efforts in other areas of the information and communication sciences are needed. In particular, I believe that our Board of Regents' recommendation that the National Library of Medicine train health professionals in the use of computer technology for more effective health care, is particularly appropriate.

Computer technology represents a powerful tool with enormous implications for health research, care, and education. Creative and dedicated health professionals are needed to provide leadership in adapting the computer technology fully to the health field. Training programs of high quality are also needed to give them these new skills in appropriate settings. Our experience with a few training grants for health professionals indicates that there is a growing need for these new skills. It has been demonstrated that such trainees are in demand and utilize computer technologies most productively.

I believe that a fiscal year 1975 funding level of $1 million would permit programs of high quality to recruit and train a significant number of qualified persons within a relatively short time.

Mr. Flood. Thank you very much, Doctor.

Dr. Cummings. Thank you.

JUSTIFICATION OF THE BUDGET ESTIMATES

NATIONAL INSTITUTES OF HEALTH

National Library of Medicine

Amounts Available for Obligation 1/

	1974 Revised	1975
Appropriation	$25,871,000	$27,738,000
Proposed supplementals*	458,000	--
Subtotal, adjusted appropriation	26,329,000	27,738,000
Real transfer to:		
"Departmental management" (For supporting the purchase of library material by the Office of the Secretary)	-20,000	--
Comparative transfer to:		
"Departmental Management" (Transfer of accounting functions from the Office of the Secretary Working Capital Fund)	-6,000	--
"Office of Assistant Secretary for Health" (Transfer of administrative support activities to the Office of the Assistant Secretary for Health)	-66,000	--
Comparative transfer from:		
"Departmental Management" (Transfer of indirect cost negotiation function to the Office of the Secretary Working Capital Fund)	7,000	--
"National Institute of General Medical Sciences" (Decentralization of scientific evaluation grants program)	10,000	--
Subtotal, budget authority	26,254,000	27,738,000
Unobligated balance, start of year	27,000	--
Unobligated balance, restored	3,494,000	--
Total, obligations	29,775,000	27,738,000

1/ Excludes the following amounts for reimbursable activities carried out by this account: 1974 - $1,200,000; 1975 - $1,500,000

* Including pay transfers (+$458,000)

Summary of Changes

1974 Estimated obligations.....................................	$29,775,000
1975 Estimated obligations.....................................	27,738,000
Net change..	-2,037,000

	1974		Change from 1974	
	Pos.	Amount	Pos.	Amount
Increases:				
A. Built-in:				
1. Annualization of 1974 Pay Cost Increases......................	--	--	--	+121,000
2. Within Grade Pay Increases.......	--	--	--	+152,000
3. FTS Rate Increase................	--	--	--	+10,000
4. Increased Cost of Services and Supplies..........................	--	--	--	+7,000
5. Payment to National Institutes of Health Management Fund......	--	--	--	+167,000
Subtotal..	--	--	--	+457,000
B. Program:				
1. Research Grants..................	--	712,000	--	+238,000
2. Regional Medical Libraries.......	--	2,601,000	--	+1,000
3. Publications Support.............	--	323,000	--	+77,000
4. Lister Hill National Center for Biomedical Communications......	18	1,975,000	--	+587,000
5. National Medical Audiovisual Center........................	100	2,631,000	--	+130,000
6. Library Operations..............	246	8,859,000	--	+820,000
7. Toxicology Information...........	16	1,563,000	--	+230,000
8. Program Direction................	53	3,403,000	--	+107,000
Subtotal..		--	--	+2,190,000
Total, increases..	--	--	--	+2,647,000
Decreases:				
A. Built-in:				
1. Annualization of Employment Savings........................	--	--	--	-100,000
B. Program:				
1. Training Grants..................	--	725,000	--	-475,000
2. Special Scientific Projects......	--	90,000	--	-15,000
3. Research.........................	--	900,000	--	-188,000
4. Library Resources................	--	2,705,000	--	-700,000
5. Regional Medical Libraries.......	--	2,929,000	--	-328,000
6. Publications Support.............	--	340,000	--	-17,000
7. Lister Hill National Center for Biomedical Communications......	18	2,752,000	--	-777,000

	1974 Pos.	1974 Amount	Change from 1974 Pos.	Change from 1974 Amount
8. National Medical Audiovisual Center	100	3,326,000	--	-695,000
9. Library Operations	246	9,754,000	--	-895,000
10. Toxicology Information	16	1,813,000	--	-250,000
11. Program Direction	53	3,647,000	--	-244,000
Total, decreases	--	--	--	-4,684,000
Total, net change	--	--	--	-2,037,000

Explanation of Changes

Increases:

A. Built In: These increases will provide $121,000 for annualization of 1974 pay cost increases; $152,000 for within-grade pay increases; $10,000 for increased cost in 1975 for using the Federal Telecommunications System; $7,000 for increased cost of services and supplies; and $167,000 payment to the NIH Management Fund for increased cost for centrally furnished services such as initial grant application review, administrative and communication services.

B. Program:

1. Research Grants - An increase of $238,000 will permit the support of 12 additional projects in the areas of medical libraries, biomedical information sciences and education and knowledge transfer.
2. Regional Medical Library Awards - An increase of $1,000 will permit the continued emphasis on developing a national network of regional medical libraries.
3. Publications Support - An increase of $77,000 will permit the continued support in the areas of critical reviews and reference tools useful to biomedical scientists and information specialists.
4. Lister Hill National Center for Biomedical Communications - An increase of $587,000 will provide support for the continued development of experimental communications systems utilizing microwave, cable television, computer-assisted instruction and satellite relay networks.
5. National Medical Audiovisual Center - An increase of $130,000 will be utilized to continue the development of new instructional media and methods which have proven to be most valuable in furthering the health education process.
6. Library Operations - An increase of $820,000 will allow this activity to continue its basic library services at approximately the FY 1974 level and permit the expansion of the MEDLARS data base to include the inputing of approximately 100,000 author abstracts into the system.
7. Toxicology Information - An increase of $230,000 will support the updating of the bibliographic file of TOXLINE and fund the expansion of information currently in the Toxicology Data Bank.
8. Program Direction - An increase of $107,000 will provide support for continued program evaluation efforts and other administrative services.

Decreases:

A. Built In: A decrease of $100,000 is for annualization of employment savings made in 1974.

B. Program:

1. Training Grants - A decrease of $475,000 is consistent with the FY 1974 policy of phasing-down the level of this activity. Support will be shifted to postgraduate training programs in computer technology for health scientists.
2. Special Scientific Projects - A decrease of $15,000 in this activity reflects a modest curtailment in the level of support for this program in FY 1975.
3. Research Grants - A decrease of $188,000 reflects reduced support for projects in the areas of medical libraries, biomedical information sciences and education and knowledge transfer.
4. Library Resources - A decrease of $700,000 reflects a reduction of 13 non-competing continuation grants in FY 1975.
5. Regional Medical Libraries - A decrease of $328,000 reflects reduced support in the development of the national regional medical libraries network.
6. Publications Support - A decrease of $17,000 reflects a reduction of support in the areas of critical reviews and reference tools utilized by biomedical scientists and information specialists.
7. Lister Hill National Center for Biomedical Communications - A decrease of $777,000 reflects reduced support in the development of experimental communications systems utilizing microwave, cable television, computer-assisted instruction and satellite relay networks.
8. National Medical Audiovisual Center - A decrease of $695,000 reflects reduced support in the development of new instructional media and methods which have proven to be most valuable in furthering the health education process.
9. Library Operations - A decrease of $895,000 will reduce the level of support for basic library services and curtail the planned expansion of the MEDLARS data base relative to the input of author abstracts.
10. Toxicology Information - A decrease of $250,000 reflects a reduced level of support for updating the TOXLINE bibliographic file and curtail the expansion of information currently in the Toxicology Data Bank.
11. Program Direction - A decrease of $244,000 will reduce program evaluation and administrative service efforts of this activity in FY 1975.

Obligations by Activity

Page Ref.		1974 Base*		1975 Estimate		Increase or Decrease		
		Pos.	Amount	Pos.	Amount	Pos.	Amount	
	Medical Library Assistance:							
243	Training	--	725,000	--	250,000	--	-475,000	A
243	Special Scientific Projects	—	90,000	--	75,000	--	-15,000	B
244	Research	--	712,000 (900,000)	--	950,000	--	+238,000	C
245	Library Resources	--	2,605,000 (2,705,000)	--	2,005,000	--	-600,000	D
246	Regional Medical Libraries	--	2,601,000 (2,929,000)	--	2,602,000	--	+1,000	E
247	Publications Support	--	323,000 (340,000)	--	400,000	--	+77,000	F
	Subtotal	--	7,056,000 (7,689,000)	--	6,282,000	--	-774,000	
	Direct Operations:							
249	Lister Hill National Center for Biomedical Communications:							G
	(a) Project contracts	--	1,423,000 (2,200,000)	--	1,985,000	--	+562,000	
	(b) Other direct	18	552,000	18	587,000	—	+35,000	
251	National Medical Audiovisual Center:							H
	(a) Project contracts	--	300,000 (995,000)	--	395,000	--	+95,000	
	(b) Other direct	100	2,331,000	100	2,421,000	—	+90,000	
251	Library Operations:							I
	(a) Project contracts	--	1,235,000 (2,130,000)	--	1,960,000	--	+725,000	
	(b) Other direct	246	7,624,000	246	7,774,000	--	+150,000	
254	Toxicology Information:							J
	(a) Project contracts	--	675,000 (925,000)	--	900,000	--	+225,000	
	(b) Other direct	16	888,000	16	908,000	--	+20,000	

Page Ref.		1974 Base* Pos.	1974 Base* Amount	1975 Estimate Pos.	1975 Estimate Amount	Increase or Decrease Pos.	Increase or Decrease Amount	
256	Review and Approval:							K
	(a) Project contracts...	--	--	--	--	--	--	
	(b) Other direct..	27	794,000	27	824,000	--	+30,000	
257	Program Direction:							L
	(a) Project contracts...	--	--	--	--	--	--	
	(b) Other direct..	53	3,403,000 (3,647,000)	53	3,702,000	--	+299,000	
	Subtotal......	460	19,225,000 (22,086,000)	460	21,456,000	--	+2,231,000	
	Total obligations (bases).........	460	26,281,000	460	27,738,000	--	+1,457,000	
	Total obligations.		(29,775,000)					

* 1974 Base - Excludes 1973 appropriation restorations. Total obligations shown in parentheses.

Explanation of Changes

A. Training Grants - A decrease of $475,000 is consistent with the FY 1974 policy of phasing-down the level of this activity. Some limited support will be given to postgraduate training programs in computer technology for health scientists.

B. Special Scientific Projects - A decrease of $15,000 relfects a modest curtailment in the level of support for this program in FY 1975.

C. Research Grants - An increase of $238,000 will permit the support of 12 additional projects in the areas of medical libraries, biomedical information sciences and education and knowledge transfer.

D. Library Resources - A decrease of $600,000 is a result of a reduction of 13 non-competing continuation grants in FY 1975. The program will continue to support 80 new awards, approximately the same level as FY 1975.

E. Regional Medical Libraries - This activity will continue to operate at its 1974 level. This will permit the continued emphasis on developing a national network of regional medical libraries.

F. Publications Support - An increase of $77,000 will permit the continued support in the areas of critical reviews and reference tools useful to biomedical scientists and information specialists.

G. Lister Hill National Center for Biomedical Communications - An increase of $597,000 will provide $10,000 for mandatory increases and $587,000 program increases to support the continued development of experimental communications systems such as microwave, cable television, computer-assisted instruction and satellite relay networks.

H. National Medical Audiovisual Center - An increase of $185,000 will provide $55,000 for mandatory increases and $130,000 for program increases. This increase will be utilized to continue the stimulation of new instructional media and methods which have proven to be most valuable in furthering the health education process.

I. Library Operations - An increase of $875,000 will provide $155,000 for mandatory increases and $720,000 for program increases. These increases will allow this activity to continue its basic library services at approximately the FY 1974 level and permit the expansion of the MEDLARS data base to include the input of approximately 100,000 author abstracts into the system.

J. Toxicology Information - An increase of $245,000 will provide $15,000 for mandatory increases and $230,000 for program increases. These increases will support the updating of the bibliographic file of TOXLINE and fund the expansion of information currently in the Toxicology Data Bank.

K. Review and Approval of Grants - An increase of $30,000 is necessary for mandatory increases. This activity will continue to provide management support for the grant and international activities administered by NLM.

L. Program Direction - An increase of $299,000 will provide $192,000 for mandatory increases (including $167,000 payment to the NIH Management Fund) and $107,000 to support program evaluation efforts and other administrative services.

Obligations by Object

	1974 Estimate	1975 Estimate	Increase or Decrease
Total number of permanent positions.......	460	460	--
Full-time equivalent of all other positions................................	26	24	-2
Average number of all employees...........	499	496	-3
Personnel compensation:			
Permanent positions.....................	$7,762,000	$8,225,000	+463,000
Positions other than permanent..........	335,000	333,000	-2,000
Other personnel compensation............	104,000	104,000	--
Subtotal, personnel compensation......	8,201,000	8,662,000	+461,000
Personnel benefits.......................	727,000	772,000	+45,000
Travel and transportation of persons......	175,000	180,000	+5,000
Transportation of things..................	26,000	34,000	+8,000
Rent, communications and utilities........	1,862,000	1,960,000	+98,000
Printing and reproduction.................	464,000	499,000	+35,000
Other services:			
Project contracts........................	5,900,000	5,240,000	-660,000
Payment to NIH Management Fund..........	1,305,000	1,472,000	+167,000
Other....................................	1,743,000	1,404,000	-339,000
Supplies and Materials....................	271,000	298,000	+27,000
Equipment.................................	1,412,000	935,000	-477,000
Grants, subsidies and contributions.......	7,689,000	6,282,000	-1,407,000
Total obligations by object.............	29,775,000	27,738,000	-2,037,000
Total obligations excluding 1973 appropriation.........................	26,281,000		

Significant Items in House and Senate Appropriations Committee Reports

Item	Action taken or to be taken
1974 Senate Report	
1. Committee directed NLM to conduct further studies on the possibility of a nominal users fee for NLM's search services. (page 63).	1. The NLM Director submitted a report on the NLM experience with user charges to the Senate Appropriations Committee in January 1974.

Authorizing Legislation

Legislation	1975 Authorized	1975 Appropriation requested
Public Health Service Act		
Section 381 - Purpose and Establishment of Library	Indefinite	$ 21,456,000
Section 394 - Grants for Training in Medical Library Sciences	1/	250,000
Section 395a - Assistance for Special Scientific Projects	1/	75,000
Section 395b - Research and Development in Medical Library Sciences and Related Fields	1/	950,000
Section 396 - Grants for Improving and Expanding the Basic Resources of Medical Libraries and Related Instrumentalities	1/	2,005,000
Section 397 - Grants for Establishment of Regional Medical Libraries	1/	2,602,000
Section 398 - Financial Support for Biomedical Publications	1/	400,000

1/ Authorization expires June 30, 1974; extension legislation is proposed.

National Library of Medicine

Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
1965	$ 3,678,000	$ 3,858,000	$ 4,058,000	$ 3,958,000
1966	9,185,000	9,185,000	9,685,000	9,685,000
1967	19,231,000	20,092,000	20,192,000	20,192,000
1968	21,162,000	18,662,000	21,162,000	19,912,000
1969	19,172,000	17,149,000	19,172,000	18,160,500
1970	22,882,000	19,682,000	19,682,000	19,682,000
1971	19,769,000	19,769,000	22,233,000	20,769,000
1972	21,981,000	22,781,000	25,086,000	24,086,000
1973*	24,994,000	28,568,000	29,068,000	28,568,000*
1974	24,994,000	25,871,000	25,871,000	26,254,000
1975	27,738,000			

*Note: This appropriation authority was the continuing resolution. The appropriations amount was the House Allowance, which was the lower of the House or Senate amounts in the first vetoed bill.

Justification

National Library of Medicine

	1974 Base*		1975 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits............	460	$8,928,000	460	$9,201,000	--	$+273,000
Other expenses............	--	17,353,000	--	18,537,000	--	+1,184,000
Total...............	460	26,281,000	460	27,738,000	--	+1,457,000

General Statement

The National Library of Medicine is the sole national institution charged with the responsibility of acquiring the world's biomedical literature and with facilitating its availability to the health science community. It is the world's largest research library in a single scientific and professional field. When the National Library of Medicine was established 138 years ago in the office of the Army's first Surgeon General, medical literature was in its infancy. Today NLM's total collections exceed 1,450,000 items.

In order to meet this explosion in biomedical literature and the rapidly increasing demands for better access to it, NLM, as the focal point within DHEW for biomedical communications activities, is developing a National Biomedical Communications Network. NLM's major efforts can best be seen within the context of this network.

NLM has initiated a nationwide, on-line, bibliographic retrieval system called MEDLINE as a general service for the biomedical community. MEDLINE is the first generally accessible, on-line, interactive information service and constitutes the first national and international telecommunications-based science information network. Over 250 institutions are now using MEDLINE in 46 states, Canada, United Kingdom, Brazil, Denmark, France, Norway, Finland, and Sweden, thereby extending its availability to most of the world's biomedical professionals.

An on-line toxicology information retrieval service, TOXLINE, has been offered to the biomedical community since October 1972. The service provides the user with remote, on-line access to a data base consisting of citations and abstracts dealing primarily with the toxicology/pharmacology of drugs, pesticides, industrial chemicals, environmental pollutants, and hazardous chemicals used in the household. Communications with the system is accomplished through terminals which link the users to a computer through the same communications network that provides NLM's MEDLINE service.

The Regional Medical Library program was developed by NLM under the Medical Library Assistance Act of 1965. Eleven Regional Medical Libraries form the backbone of the Biomedical Communications Network. Ten Regional Medical Libraries are funded by NLM throughout the country to provide interlibrary loan service, reference services, education and consultation, and

MEDLINE and TOXLINE to health science libraries in their regions. Through the Regional Medical Library Program, NLM has developed an effective means of sharing biomedical information resources throughout the nation so that all libraries, from NLM to the smallest hospital libraries, will be able to have access to the nation's biomedical information.

NLM has also developed new modes of biomedical communications. For example, the Library's Lister Hill National Center for Biomedical Communications has developed a satellite communications network in Alaska. Satellite communications are being used in remote villages to allow native health aides to communicate via satellite radio with physicians at Alaska Native Health Service Unit Hospitals, provide continuing education to health aides, nurses, and physicians, and to allow communication between hospitalized patients and their families. A preliminary evaluation of this experiment has documented a 400 percent increase in the number of village patients that are now being treated with the advice of a physician as compared to previous years when unreliable radio was used.

Other biomedical communications experiments include the use of more innovative educational techniques such as audiovisuals and multimedia instructional packages, a computer-assisted instruction network for medical education, a medical interactive television network to link rural hospitals and medical centers, and a cable television network to bring health education to the urban poor and elderly. Each of these accomplishments is related to the development of a national network for biomedical communications.

The FY 1975 budget request will allow progress to be made in improving the nation's biomedical communications, especially in improving the manner in which library and information services are performed. This achievement results in increases of productivity in medical education and health care delivery.

*Excludes 1973 appropriation restorations.

Medical Library Assistance Programs

Authorizing Legislation: Health Programs Extension Act, 1973 (P.L. 93-45)

	1974 Base*		1975 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits...........	--	--	--	--	--	--
Other expenses...........	--	$7,056,000	--	$6,282,000	--	$-774,000
Total...............	--	7,056,000	--	6,282,000	--	-774,000
Subactivities:						
Training.............	--	725,000	--	250,000	--	-475,000
Special Scientific Projects...........	--	90,000	--	75,000	--	-15,000
Research.............	--	712,000	--	950,000	--	+238,000
Library Resources....	--	2,605,000	--	2,005,000	--	-600,000
Regional Medical Libraries..........	--	2,601,000	--	2,602,000	--	+1,000
Publications Support.	--	323,000	--	400,000	--	+77,000
Total..............	--	7,056,000	--	6,282,000	--	-774,000

The programs authorized by the Medical Library Assistance Act of 1965, as amended, are designed to meet national needs for better health information services through health library resources and facilities, trained manpower and improved health communications technology.

* Excludes 1973 appropriation restorations.

Training

	1974 Base*		1975 Estimate		Increase or Decrease	
	No. of Awards	Amount	No. of Awards	Amount	No. of Awards	Amount
Non-competing continuation grants............	9	$725,000	4	$250,000	-5	$-475,000
New grants................	--	--	--	--	--	--
Total..............	9	725,000	4	250,000	-5	-475,000

The training grants program has supported since 1966 innovative graduate and postgraduate curricula for the education and training of medical librarians, biomedical communication specialists, medical historians, and other professional personnel required for health science communications research and services. Approximately 600 such trainees have been supported during the past eight years. The graduates of these programs have become directors or professional staff members of biomedical communications programs, medical libraries, and health science information systems throughout the United States.

In FY 1974 a policy was established that called for an overall reduction in the level of the training grants program on the basis that there was no longer a critical shortage of medical librarians. Program emphasis has, therefore, been directed to supporting postgraduate training programs in computer technology for health scientists.

Several grants were made in FY 1974 in the areas of medical librarianship, biomedical communications, and information science. The remaining grants were designed to train individuals who will promote the effective integration of computer technology into all phases of clinical medicine--teaching, practice, and research.

*Excludes 1973 appropriation restorations

Special Scientific Projects

	1974 Base*		1975 Estimate		Increase or Decrease	
	No. of Awards	Amount	No. of Awards	Amount	No. of Awards	Amount
Non-competing continuation grants............	2	$36,000	2	$53,000	--	$+17,000
New grants................	1	54,000	1	22,000	--	-32,000
Total...............	3	90,000	3	75,000	--	-15,000

Special Scientific Projects are designed to enable highly qualified senior health professionals to work full-time to produce comprehensive reviews and treatises in their areas of specialty.

The objectives of the program are to encourage the scholarly exploration of the total effects upon our society stemming from advances in the health sciences, to gain some insight into the nature and effects of these influences and to attempt to assess their implications.

Although the scholars supported by Special Scientific Projects are not engaged in laboratory research, their work is to analyze and transmit such research findings.

For example, a project supported by this program is to write a comprehensive monograph on the discovery, classification, and treatment of infectious diseases and the development of preventive medicine and public health measures for their control.
*Excludes 1973 appropriation restorations.

Research

	1974 Base*		1975 Estimate		Increase or Decrease	
	No. of Awards	Amount	No. of Awards	Amount	No. of Awards	Amount
Non-competing continuation grants...........	18	$598,000	8	$226,000	-10	$-372,000
New grants...............	2	114,000	24	724,000	+22	+610,000
Total..............	20	712,000	32	950,000	+12	+238,000

The purpose of the research grants program is to provide assistance for investigative projects in the field of medical library sciences, and for the development of new techniques, systems, and equipment for processing, storing, retrieving, and distributing health sciences information.

Some 300 research, development, and demonstration projects have been supported through this program since 1966 and in FY 1975 thirty-two projects will be supported in the areas of: (1) medical libraries and librarianship; (2) biomedical information sciences and services; (3) education and knowledge transfer; and (4) the history of medicine.

Projects supported to date have resulted in a better understanding of how health information is sought and delivered to health scientists. Computer-based medical diagnosis and its application to medical decision making was studied. Projects were supported to investigate the educational needs of health sciences library manpower and to test and evaluate various types of training programs for hospital librarians. The cost-effectiveness of different methods of selectively disseminated biomedical literature is another subject for investigation.
*Excludes 1973 appropriation restorations.

Medical Library Resources

	1974 Base*		1975 Estimate		Increase or Decrease	
	No. of Awards	Amount	No. of Awards	Amount	No. of Awards	Amount
Non-competing continuation grants............	43	$1,414,000	30	$756,000	-13	$-658,000
New grants................	79	1,191,000	80	1,249,000	+1	+58,000
Total..............	122	2,605,000	110	2,005,000	-12	-600,000

Medical Library Resource grants are designed to assist in the establishment, improvement, and expansion of the nation's health science libraries, and to encourage increased community support for the local library. Grants for a one-year period with a maximum budget of $3,000 are made to health institutions which demonstrate a need to establish basic collections and services. The 1975 budget estimate will allow the support of 30 such grants. Grants are also made to institutions with existing health science libraries for the support of projects designed to make the growing scientific literature more rapidly accessible to health professionals throughout the United States. The 1975 budget estimate will allow the support of 50 such grants. These projects are supported for a maximum of three years with a ceiling of $200,000 for any budget period. Funded applications include cooperative programs in which a strong resource library undertakes to provide training, consultation and loan services for the small community hospitals, clinics and other facilities. Funds will support studies which seek to speed the delivery of services through the use of modern communication devices and automation techniques; and projects which, after an assessment of needs of the health professionals, strengthen the information resources of an institution.

These grants have supported projects designed to improve the technical functions of the library and to directly improve or expand services to the library's health professional user. They also have supported the acquisition of core journals and other basic informational materials needed in community health care institutions. These institutions have made a firm commitment to maintain, with local funds, a meaningful level of library support during and after the grant period. Grants have also been made to biomedical libraries in larger hospitals and academic health institutions. These latter grants have supported cooperative programs in which relatively strong libraries undertake to assist small hospital libraries through consultation, training, and other services.

*Excludes 1973 appropriation restorations.

Regional Medical Libraries

	1974 Base*		1975 Estimate		Increase or Decrease	
	No. of Awards	Amount	No. of Awards	Amount	No. of Awards	Amount
Non-competing continuation grants...........	10	$2,601,000	10	$2,602,000	--	$+1,000
New grants..............	--	--	--	--	--	--
Total.............	10	2,601,000	10	2,602,000	--	+1,000

The goal of this program is to develop a national network of regional medical libraries with the necessary depth and scope to supplement the services of other medical libraries in their designated region. Backup library services in the form of interlibrary loans and sophisticated reference services are now available.

The FY 1975 request will allow the library to continue the contract support for the ten active Regional Medical Libraries (RML's). The RML's have become well utilized over the years due primarily to three factors:

1. Greatly increased reliance on the RML's by health professionals has resulted in their becoming increasingly aware of the availability of interlibrary loan service from these regional libraries.

2. The continued development of the NLM's on-line bibliographic retrieval service, MEDLINE, will afford direct and greatly improved access by RML clients to a data base which is most relevant to a health professional's requirements.

3. Many of the proposed national health care systems will place increased demands upon the Regional Medical Library Network. For example, Area Health Education Centers, Health Maintenance Organizations, National Health Insurance, and Professional Standards Review Organizations will place additional responsibilities on the health professionals. These individuals will require additional information resources and services to adequately fulfill these roles.

The concept of the Regional Medical Library System is built on resource sharing. This means that each library does not have to acquire and hold all the information resources within its confines. Rather such resources are identified and made available to be shared with other libraries. The National Library of Medicine, as part of its operation, provides much of this information through its computer based programs (MEDLINE, SERLINE, CATLINE, TOXLINE, etc.).

*Excludes 1973 appropriation restorations.

Publications

	1974 Base*		1975 Estimate		Increase or Decrease	
	No. of Awards	Amount	No. of Awards	Amount	No. of Awards	Amount
Non-competing continuation grants...........	11	$139,000	12	$194,000	+1	$+55,000
New grants..............	9	184,000	6	206,000	-3	+22,000
Total.............	20	323,000	18	400,000	-2	+77,000

Publication grants provide support for the preparation or publication of abstracts, bibliographies, handbooks, critical reviews, and translations. The publications repackage information to make it more available to health scientists, educators, and practitioners.

Grants are made to individual scientists or to public or nonprofit institutions of higher education on behalf of such scientists. Projects supported by the program are those of scientific merit which, because of their specialized subject matter, have a limited market thus precluding their publication by a commercial publisher.

Approximately one-half of FY 1975's appropriation request of $400,000 represents commitments for the support of work begun in prior fiscal years. The remaining amount will be used to support approximately six new awards at an estimated average cost of $35,000 each. The projects selected will be those which related to the improvement of health practices and the delivery of health services. Awards in the following general areas will be emphasized: a review of the latest techniques in the practice of family medicine; reviews which would summarize and interpret modern educational techniques; reference manuals or similar guidelines for librarians in community hospitals, etc.

In FY 1974 grants were concentrated in the areas of critical reviews and reference tools useful to biomedical scientists and information specialists. Examples of the projects funded were a study of the development of a highly innovative curriculum at a major medical school; an Atlas of Protein Structure, which will serve as a reference tool for geneticists and other scientists concerned with the structure, function, and genetics of proteins; and a project aimed at the development and publication of a comparative mammalian histological nomenclature which would find universal acceptance among microanatomists and histopathologists.

*Excludes 1973 appropriation restorations.

Direct Operations

Authorizing Legislation: Section 301 and Part I of the Public Health Service Act

	1974 Base*		1975 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits...........	460	$8,928,000	460	$9,201,000	--	$+273,000
Other expenses...........	--	10,297,000	--	12,255,000	--	+1,958,000
Total..............	460	19,225,000	460	21,456,000	--	+2,231,000
Subactivities:						
Lister Hill National Center for Biomedical Communications........	18	1,975,000	18	2,572,000	--	+597,000
National Medical Audiovisual Center....	100	2,631,000	100	2,816,000	--	+185,000
Library Operations......	246	8,859,000	246	9,734,000	--	+875,000
Toxicology Information..	16	1,563,000	16	1,808,000	--	+245,000
Review and Approval.....	27	794,000	27	824,000	--	+30,000
Program Direction.......	53	3,403,000	53	3,702,000	--	+299,000
Total................	460	19,225,000	460	21,456,000	--	+2,231,000

*Excludes 1973 appropriation restorations.

Lister Hill National Center for Biomedical Communications

	1974 Base*		1975 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits............	18	$409,000	18	$419,000	--	$+10,000
Other expenses............	--	1,566,000	--	2,153,000	--	+587,000
Total...............	18	1,975,000	18	2,572,000	--	+597,000

The Lister Hill Center encourages the application of advanced computer and communications technologies to the solution of biomedical information problems. Microwave, cable television, data communications, computer-assisted instruction, and satellite relay networks are among the experimental and operational systems supported by the Center.

Satellite: For more than 2 1/2 years the Center has supported an experimental voice network linking over twenty Alaskan native villages with Indian Health Service hospitals and medical centers in Alaska. The network, which utilizes a NASA Applications Technology Satellite (ATF-1), has demonstrated the benefits of improved voice communication for the health care of widely dispersed populations. An evaluation of the project has shown a fourfold increase in the number of patients being treated with a doctor's advice since the experiment began. On the basis of the network's success, the Lister Hill Center has provided the Indian Health Service with cost projections for other possible networks involving terrestial and satellite links.

The April 1974 launch date of NASA's Applications Technology Satellite-F (ATS-F) will climax a period of extremely close cooperation by the Lister Hill Center, other Federal agencies, regional commissions, and major medical centers. Under the Center's direction, seven satellite telecommunications terminals have been installed in the states of Washington and Alaska to support experiments using the satellite. The experiments will evaluate the effectiveness of live television and consultation between physicians at Indian Health Service Hospitals and two small, remote clinics in Alaska manned by health aides and other "physician-extender" personnel.

In 1975, the ATS-1 remote medical consultation network will be expanded to support the ATS-F program. The communications link will connect native village clinics, medical centers, and the Tanana (Alaska) Hospital with the Indian Health Service information service in Tucson, Arizona. Through this communications link the native village clinics will be able to obtain up-to-date medical records on all listed village personnel. This system will provide current information about patients to assist the health professional in patient management.

Alaskan village personnel will be trained to operate the satellite terminals provided for the ATS-F experiment. Following completion of a detailed training program a ten-month experiment will be conducted to evaluate the use of satellites to support health care and medical education in remote locations.

The University of Washington will use the ATS-F satellite to provide education for first-year medical students at the University of Alaska, and for students taking their preceptorship under physicians in Omak, Washington.

Interactive Television: Since June 1970 the Center has been engaged in testing the hypothesis that interactive television is an effective medium for providing continuing education and medical services in rural settings. Work began with the conversion of a leased microwave television link between Dartmouth College and the Claremont, New Hampshire General Hospital. The link has since been expanded to provide a similar capability to the University of Vermont Medical School. More recently, with the construction of a mobile van-mounted unit and appropriate receiving antennas, the network has been joined by a state prison, a community hospital in Vermont, and a vocational technical college in Claremont.

Approximately two-thirds of the programming is devoted to health education and one-third to patient care. A typical week's operation encompasses 44 program hours, which correspond to over 400 viewer hours.

FY 1974 is the last year of full Federal funding for network operations. The Center already has verified that the network is an effective medium for the delivery of continuing medical education and other services. What remains to be proven is that it can be operated on a self-sustaining basis. To that end, in 1975 the Center will help reorient the network from a research project to an aggressive, cost-conscious business type of operation.

Computer-Assisted Instruction (CAI): In FY 1972 the Lister Hill Center initiated a national CAI network for the inter-institutional sharing of educational resources. Three university medical centers with strong CAI development programs were connected to the NLM national communications network. Their computers and programs were then offered to institutions that would integrate the educational programs into their own curricula, evaluate them, and produce additional units of instruction. In FY 1974, seventy-six hospitals, medical and dental schools, and similar institutions became users of the CAI services. The national CAI network averaged over 12,000 user interactions per month. Beginning in January 1974, when the Center found it necessary to require users to pay a share of the communications costs of the network, utilization fell off somewhat. In FY 1975 the charge to users will be increased. To help avoid further reductions in the use of the CAI network, the Center will study ways to make evaluated CAI programs available for sharing by identified user populations at a most reasonable cost.

Cable TV: The Lister Hill Center believes that improved communications between users and providers of health services can help reduce some of the health problems caused by isolation. During FY 1974, the LHC introduced the concept of "cable television for health" to the elderly population of a public housing unit in East Harlem, New York City. During FY 1974 cable was installed in Gaylord White Apartment and outlets provided in selected viewing areas. Cooperation between Mt. Sinai, Union Settlement and the tenants has resulted in the development of special programming designed to increase awareness and involvement of this population.

In 1975 the Center plans to expand video programming to make it interactive. A contract will be initiated to poll user desires and modify programming accordingly. The Center will begin an evaluation of community interaction as an effective means of health education for the geriatric population, and will begin implementing a plan to provide psychiatric services over the cable system.

*Excludes 1973 appropriation restoration.

National Medical Audiovisual Center

	1974 Base*		1975 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits............	100	$1,793,000	100	$1,848,000	--	$+55,000
Other expenses............	--	838,000	--	968,000	--	+130,000
Total...............	100	2,631,000	100	2,816,000	--	+185,000

The principal goal of the National Medical Audiovisual Center is to develop a national program to improve the quality and use of biomedical audiovisuals in health professional schools and throughout the biomedical community. The Center's mission is to strengthen the information and educational processes within the health professions.

The National Medical Audiovisual Center encompasses seven major program areas: a clearinghouse to assemble, catalog, and disseminate data on audiovisuals, evaluation and acquisition of mediated instructional materials, distribution of audiovisuals, advisory services, training in the use of audiovisuals, applied research in instructional technology and development of prototype instructional media programs.

In FY 1975, NMAC will work to improve the identification, cataloging, and indexing of instructional media. Specifically, reference to available media will be enhanced through augmentation of NLM information systems. Reference services will become more responsible to the demands of faculty, students, and other health professional users of learning resource centers. The distribution of instructional materials, whether through film loans, broadcast transmission, or video-tape duplication, will be concentrated on those materials which have proven to be most valuable in furthering the health education process.

NMAC will continue to concentrate its support in key areas of educational change and institutional need. Cooperation with national professional organizations and health professional school faculties will continue to provide specialized support for developing the curriculum content of audiovisual media. In addition, agreements with organizations such as the American Association of Medical Colleges and the American Association of Dental Schools will provide NMAC with continuing feedback on the actual utility of media which have been developed.

In FY 1974, NMAC, identified, cataloged, and indexed effective audiovisual instructional media. It produced and acquired for distribution or sale instructional media not otherwise available from professional or commercial sources. By the development of modular instructional units, and the provision of advisory, training, and information services, it also stimulated the development of new instructional media and methods at varied health professional schools.

In conjunction with the Health Resources Administration, it continued to support an agreement with the Association of American Medical Colleges and the American Association of Dental Schools under which those organizations help determine curriculum appropriateness and identify and coordinate subject matter for review, design, and development of instructional media. Through cooperative efforts such as this, NMAC not only received the benefit of outside expertise but at the same time informed the health education community about the advantages to be gained from using audiovisuals.

*Excludes 1973 appropriation restorations.

Library Operations

	1974 Base*		1975 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits...........	246	$4,418,000	246	$4,573,000	--	$+155,000
Other expenses...........		4,441,000	--	5,161,000	--	+720,000
Total..............	246	8,859,000	246	9,734,000	--	+875,000

Library Operations selects, acquires, indexes, catalogs, and preserves the world's biomedical publications. It provides access to the material through manual and machine-produced bibliographies; furnishes reference and loan services; prepares and publishes indexes, catalogs, and other publications for use of the biomedical community; operates the Library's in-house computer facility; manages the Library component of the Biomedical Communications Network; and serves as the Regional Medical Library for the Mid-Atlantic Region of the United States.

The FY 1975 budget request will allow Library Operations to continue its basic services at approximately the FY 1974 levels: acquiring 100,000 serial pieces and 26,000 monographs; indexing 225,000 articles; publishing 28 recurring bibliographies; binding 30,000 volumes; and providing 175,000 interlibrary loans. It also will provide 90,000 reader services.

FY 1975 funds will provide for additional input costs for the planned expansion of the MEDLARS data base to include author abstracts. Inclusion of abstracts will provide increased capability for text searching and will enable users to retrieve more specific medical information that is now unavailable. Approximately 100,000 abstracts will be entered into the system by the end of FY 1975.

Cooperative projects with other national and federal libraries will be expanded in FY 1975. A cooperative effort with the Federal Library Committee, currently in experimental stages, will link the NLM with a national on-line cataloging system maintained by the Ohio College Library Center.

In FY 1975 the NLM plans to further increase the capabilities of its computer facility. Continued expansion of the MEDLARS II system will be undertaken with audiovisual information added. Plans are nearing completion for the operation of TOXLINE in-house. These additional uses of the computer facility will require that a second central processor and associated peripheral equipment be installed.

FY 1974 has been characterized by continued rapid growth of the new, innovative services instituted by Library Operations; expansion of the number of services available; upgrading of the equipment used; imposition of user charges; and most importantly, achievement of full operational status of the second generation Medical Literature Analysis and Retrieval System, MEDLARS II.

MEDLINE services have made substantial gains during FY 1974 both in the number of user institutions, up 50 percent to 250, and in the number of searches performed, up 40 percent to 225,000. MEDLINE is now available in 46 states, ten Canadian Centers, Sweden, United Kingdom, France, Finland, Norway and Denmark and, in cooperation with the Pan American Health Organization, in San Paulo, Brazil. In return for MEDLINE services most of these centers provide the equivalent of $250,000 worth of foreign language indexing for input into the MEDLARS data base.

Library Operations has continued to expand its on-line services through the implementation of new data bases. Three such services include: SDILINE, which is a complete file of those citations for the next month's Index Medicus; CATLINE, which provides access to catalog data on the monographic collection of the NLM; and SERLINE, which offers access to descriptive information on the 5,500 major biomedical serial titles and data regarding what libraries hold those titles.

The widespread acceptance of MEDLINE and projections of its continued rapid growth strongly indicated a need to establish some form of MEDLINE user charges for the twofold purpose of establishing a degree of management control over the growth of the system and to provide a suitable funding alternative. The charge has been levied by the network operator and is used to offset a portion of the communication costs. In FY 1974 an estimated $220,000 will be collected by the contractor from the users to offset a portion of the cost of providing the communication network services in regions remote from major urban areas. An estimated $290,000 will be collected in FY 1975. These charges will permit the NLM to maintain the MEDLINE system without serious fiscal problems which could occur if usage should continue to grow.

Other activities undertaken in FY 1974 include the implementation of a computerized management file to provide on-line tracking and control over the acquisition process; and experimental study with the British Lending Library which will provide certain documents not available at the NLM; and completion of plans to provide access to the catalog file dating back to 1965 directly from the computer.

Library Operations continues to prepare and publish the monthly Index Medicus, the yearly Cumulated Index Medicus, 28 specialized recurring bibliographies in the field of medicine in collaboration with federal agencies and professional medical societies, and the Abridged Index Medicus which has been developed for the individual practitioner and small hospital libraries. *Excludes 1973 appropriation restorations.

Toxicology Information

	1974 Base*		1975 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits...........	16	$454,000	16	$469,000	--	$+15,000
Other expenses...........	--	1,109,000	--	1,339,000	--	+230,000
Total..............	16	1,563,000	16	1,808,000	--	+245,000

The Toxicology Information Program (TIP) organizes toxicology information from scattered, diverse sources into computerized storage and retrieval systems. The program provides the health community with ready access to toxicology information from the published scientific literature and from the files of governmental, industrial and academic organizations.

Automated Systems

In 1974, TIP continued to develop and maintain TOXLINE (formerly called TOXICON), its on-line bibliographic information retrieval service. The system contains 300,000 records consisting of citations, index terms and abstracts from the published toxicology literature. The TOXLINE file includes data on pesticides, environmental toxins, pharmaceuticals, and hazardous household and industrial products. It also covers the treatment of poisoning and drug abuse. At the end of its first year of operation, over 70 organizations paid $46,000 for use of TOXLINE, and 110 individuals had been trained in its proper use.

In collaboration with the University of Rochester and the Dartmouth Medical School, TIP continued to computerize selected portions of the well-known handbook, Clinical Toxicology of Commercial Products, for use in an on-line TOXLINE Product Composition File. It also initiated a major new effort to develop a compound-oriented Toxicology Data Bank (TDB), which will contain chemical, biomedical and environmental information for each chemical substance. Estimates call for the TDB eventually to contain information on 3,000-4,000 hazardous substances to which large numbers of people are exposed.

In 1975 TIP will to operate and maintain TOXLINE in the NLM computer. It will update the bibliographic file of TOXLINE on a regular basis and increase the information in the Toxicology Data Bank to cover 1,000 chemical substances.

Specialized Products and Files Based on the Published Literature

In 1974, TIP will publish Volume II of Drug Interactions - An Annotated Bibliography with Selected Excerpts, which contains 1,200 drug interaction excerpts. At a time of increasing use of new and potent drugs in the treatment of disease, information on interactions between drugs is more vital than ever to professionals engaged in research and health care.

TIP also continued work on its monthly abstract journal and companion computer tape service, Abstracts on Health Effects of Environmental Pollutants. This information service helps meet the needs of workers in another vital area--the study of the relationship of environmental pollution to the nation's health.

The "Common Data Base," a computerized file containing structual and nomenclature information on biomedically important compounds, has been incorporated in part into an on-line, interactive chemical dictionary file, the TOXLINE Chemical Dictionary (TCD). This file now consists of over 60,000 chemical substance records containing molecular formulas, synonyms, and other data which enable a user to search TOXLINE for information on a single chemical substance known by many names in the literature. In effect, the file greatly increases the usefulness of all other toxicology information services.

Plans for 1975 include maintenance of the TCD file and continued input of selected references from the MEDLARS data base for the computer-generated abstract journal.

Collaborative Activities with Other Organizations

Early in 1974, the Assistant Secretary for Health created a special DHEW committee to coordinate toxicology related activities throughout the Department. In the third quarter of 1974, the Committee vested TIP with the responsibility for developing and managing department-wide toxicology data systems. As part of the effort to meet its increased responsibilities, TIP negotiated a number of new agreements with other Federal agencies to provide information services on a reimbursable basis. Under prior arrangements, TIP continued to obtain tape files from the American Chemical Society and the American Society of Hospital Pharmacists. During a meeting of the Organization for Economic Co-operation and Development (OECD), TIP proposed the development of an international exchange system for toxicity data. Plans in 1975 call for the evaluation of methods for implementing such a system, and for continuation of all other activities as in 1974.

Toxicology Information Response Center

TIP continued to support the Toxicology Information Response Center at the Atomic Energy Commission's Oak Ridge National Laboratory. On request, the Center will perform approximately 350 literature searches in various areas of toxicology for the scientific community. A $50 fee is charged with billings and collections provided by the National Technical Information Service (NTIS) of the Department of Commerce. The NTIS also distributes to the public those search bibliographies which have widespread scientific interest.

Through small contracts, the Center sponsored several state-of-the-art reviews on topics of current interest in the field of toxicology. These reviews were prepared by selected experts and were published in such journals as Environmental Health Perspectives or through the NTIS.

TIP will continue to support the publication of state-of-the-art reviews and bibliographies in whatever areas of toxicology may be of particular interest to the biomedical community.
*Excludes 1973 appropriation restorations.

Review and Approval

	1974 Base*		1975 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits...........	27	$660,000	27	$680,000	--	$+20,000
Other expenses...........	--	134,000	--	144,000	--	+10,000
Total..............	27	794,000	27	824,000	--	+30,000

Review and Approval provides staff to manage the six grant programs authorized by the Health Programs Extension Act of 1973, as well as international activities of the NLM funded by the Scientific Activities Overseas appropriation.

Functions include the preparàtion and processing of grant applications for review committees and the Board of Regents of the National Library of Medicine. In an average year the staff handles 450 to 500 applications, about twenty five percent of which are non-competing renewal applications. Review and Approval also provides assistance to applicants in interpreting program policies; performs continuing program planning, analysis and evaluation; and provides overall grants management and direction.

* Excludes 1973 appropriation restorations.

Program Direction

	1974 Base*		1975 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits...........	53	$1,194,000	53	$1,212,000	--	$+18,000
Other expenses..........	--	2,209,000	--	2,490,000	--	+281,000
Total.............	53	3,403,000	53	3,702,000	--	+299,000

This activity provides the program leadership and centralized administrative support necessary for the coordinated operation of all NLM activities.

Program Direction provides support for the immediate Office of the Director, Office of Administration, Office of Inquiries and Publications Management, and payment to the National Institutes of Health Management Fund for centrally furnished services.

In fiscal years 1974 and 1975 Program Direction is giving increased emphasis to meaningful program analysis and evaluation of the impact of NLM support, as is evidenced by the creation of a new Office of Program Analysis and Legislation. Under this activity is located the overall direction and coordination of the construction of the Lister Hill National Center for Biomedical Communications. Planning funds for the architectural and engineering design of this new facility have been apportioned and a firm is engaged in this work. The initial design concept drawings have been completed and the final bid documents necessary for the actual construction will be completed by the end of December 1974.

*Excludes 1973 appropriation restorations.

NATIONAL INSTITUTES OF HEALTH

National Library of Medicine

Program Purpose and Accomplishments

Activity: Training Grants (Medical Library Assistance Extension Act, Section 394)

1974		1975		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
--	$725,000	1/	--	$250,000

Purpose: The training grants program has supported since 1966 innovative graduate and postgraduate curricula for the education and training of medical librarians, biomedical communications specialists, medical historians, and other professional personnel required for health science communications research and services.

Explanation: Grants are made to nonprofit institutions and individuals qualified to conduct the proposed training activities.

Accomplishments in 1974: Program emphasis has been redirected from pre-doctoral training grants to supporting postgraduate training programs in computer technology for health scientists. The nine grants funded in FY 1974 supported the training of forty-one individuals. Five grants were designed to train individuals who will promote the effective integration of computer technology into all phases of clinical medicine--teaching, practice, and research. Single grants were made in the areas of medical librarianship, biomedical communications and information science.

Objectives for 1975: Grants will be made in FY 1975 to support postgraduate training programs in computer technology for health scientists.

1/ Authorization expires June 30, 1974; extension legislation is proposed.

NATIONAL INSTITUTES OF HEALTH

National Library of Medicine

Program Purpose and Accomplishments

Activity: Special Scientific Projects (Medical Library Assistance Extension Act, Section 395(a)

1974		1975		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
--	$90,000	1/	--	$75,000

Purpose: Special Scientific Projects support distinguished scholars in the full-time analysis and documentation of major advances in the health sciences. The results are published as book-length monographs which serve to make selected areas of biomedical information more accessible.

Explanation: Grants are awarded to scholars and to public or nonprofit institutions on behalf of such scholars.

Accomplishments in 1974: An example of a project supported in FY 1974 is a study of how the democratic government that followed the French Revolution coped with the challenge that "the state owes each indigent patient complete, prompt, and free medical care." The study analyzed the philosophy of the citizen's right to health care and the medical, financial and administrative problems associated with that philosophy. The French government in 1789 faced responsibilites that strongly resemble the problems which the American government faces today. The terminal phases of the research were supported in 1974 and the results will be published as a book-length monograph.

Objectives for 1975: Examples of projects to be supported in FY 1975 are a monograph on the pathophysiology of pulmonary disease, and a comprehensive monograph on the discovery, classification, and treatment of infectious diseases and the development of preventive medicine and public health measures for their control.

1/ Authorization expires June 30, 1974; extension legislation is proposed.

NATIONAL INSTITUTES OF HEALTH

National Library of Medicine

Program Purpose and Accomplishments

Activity: Research and Development (Medical Library Assistance Extension Act, Section 395(b))

1974		1975		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
--	$712,000	1/	--	$950,000

Purpose: The purpose of the research grants program is to provide assistance for investigative projects in the field of medical library sciences, and for the development of new techniques, systems, and equipment for processing, storing, retrieving and distributing health sciences information.

Explanation: Grants are awarded to public or private nonprofit institutions on behalf of a principal investigator.

Accomplishments in 1974: A grant was made in FY 1974 to study the efficacy of centralized processing for a group of medical libraries. Another project led to the publication of a handbook on The Ocular Fundus in Systemic Disease. The program also supported a team of information specialists and physicians in the investigation of computer-aided decision making.

Objectives for 1975: Thirty-two projects will be supported in the areas of: (1) medical libraries and librarianship; (2) biomedical information sciences and services; (3) education and knowledge transfer; and (4) the history of medicine. Potential projects will include studies of the utility of modern information services as they relate to the library; the possible new roles of the library within its institutional framework; the resultant potential new roles of librarians; computer-based information systems and their cost/benefit analysis; the impact of new information systems on health practitioners; the development of new information systems on health practitioners; the development of new information handling systems; and the educational process, curriculum design, and educational technologies as applied to health education.

1/ Authorization expires June 30, 1974; extension legislation is proposed.

NATIONAL INSTITUTES OF HEALTH

National Library of Medicine

Program Purpose and Accomplishments

Activity: Medical Library Resource Grants (Medical Library Assistance Extension Act, Section 396)

1974		1975		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
--	$2,605,000	1/	--	$2,005,000

Purpose: Funds are used to assist in the establishment, improvement, and expansion of the nation's local health science libraries, and to encourage financial support for such libraries by the communities in which they are located.

Explanation: One year, non-renewable improvement grants for up to $3,000 are made to establish basic health information units, usually in hospitals. Project grants of up to three years' duration are made to facilitate the dissemination of health information and to introduce or demonstrate new technologies in information science.

Accomplishments in 1974: The grants supported cooperative programs in which strong libraries assisted smaller hospital libraries through consultation, training, and other services. The program also supported the use of modern communications devices and automation techniques to expedite the delivery of library services; and the improvement of physical facilities to provide more efficient storage and retrieval of information. Additional awards supported the acquisition of core libraries and other basic materials by community health care institutions.

Objectives for 1975: The resource grants program will continue to complement the NLM's Regional Medical Library program by upgrading the resources of local libraries within the regions. The program will support formal agreements among local hospitals to achieve the objectives of greater cooperation. Such agreements, by providing for planned, coordinated acquisition of library materials, will help eliminate the waste that occurs when each institution attempts to have a complete collection of its own. Thirty non-competing grants and 80 new grants will be awarded in FY 1975 to support the acquisition of both print and audiovisual media as well as library services necessary to meet the information needs of the community.

1/ Authorization expires June 30, 1974; extension legislation is proposed.

NATIONAL INSTITUTES OF HEALTH

National Library of Medicine

Program Purpose and Accomplishments

Activity: Regional Medical Library Awards (Medical Library Assistance Extension Act, Section 397)

1974		1975		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
—	$2,601,000	1/	--	$2,602,000

Purpose: The Regional Medical Library Program provides a national network of medical libraries with the necessary resources and services to act as backup to and supplement for other medical libraries within a designated region.

Explanation: Services and resources provided by the ten Regional Medical Libraries include interlibrary loans, basic reference services, management and planning for the biomedical communications network within their region and educational and consultative services. The ten libraries are selected because of the scope and coverage of their collections and their ability to supplement the needs of the medical libraries within their regional component.

Accomplishments in 1974: The Library renewed its contracts with each of the Regional Medical Libraries during FY 1974, and over 500,000 interlibrary loans were made. The number of MEDLINE user institutions increased by 50% to 250 during the fiscal year.

Objectives for 1975: Continued funding of the ten Regional Medical Libraries will be made in FY 1975. The number of services provided will increase substantially due to increased exposure of the available RML services, expansion of available NLM data bases, and the prohibitive high cost associated with the purchase of many serials and monographs by the smaller libraries. Continued emphasis will be placed on improving and strengthening the national network and on making available health information to improve patient care and health education.

1/ Authorization expires June 30, 1974, extension legislation is proposed.

NATIONAL INSTITUTES OF HEALTH

National Library of Medicine

Program Purpose and Accomplishments

Activity: Biomedical Scientific Publications (Medical Library Assistance Extension Act, Section 398)

1974		1975		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
--	$323,000	1/	--	$400,000

Purpose: Publication grants provide support for the preparation or publication of abstracts, bibliographies, handbooks, critical reviews, and translations. The publications repackage information to make it more available to health scientists, educators, and practitioners.

Explanation: Grants are made to individual scientists or to public or nonprofit institutions of higher education on behalf of such scientists. Projects supported by the program are those of scientific merit which, because of their specialized subject matter, have a limited market that precludes publication by a commercial publisher.

Accomplishments in 1974: Grants were concentrated in the areas of critical reviews and reference tools useful to biomedical scientists and information specialists. Projects supported in FY 1974 included a study of the development of a highly innovative curriculum at a major medical school; an Atlas of Protein Structure, which will serve as a reference tool for genetics of proteins; and a project aimed at the development and publication of a comparative mammalian histological nomenclature which would find universal acceptance among microanatomists and histopathologists.

Objectives for 1975: Approximately one-half of FY 1975's appropriation request of $400,000 represents commitments for the support of work begun in prior fiscal years. The remaining amount will be used to support approximately six new awards at an estimated average cost of $35,000 each. The projects selected will be those which relate to the improvement of health practices and the delivery of health services. Awards in the following general areas will be emphasized: a review of the latest techniques in the practice of family medicine; reviews which would summarize and interpret modern educational techniques; reference manuals or similar guidelines for librarians in community hospitals, etc.

1/ Authorization expires June 30, 1974; extension legislation is proposed.

NATIONAL INSTITUTES OF HEALTH

National Library of Medicine

Program Purpose and Accomplishments

Activity: Lister Hill National Center for Biomedical Communications (Public Health Service Act, Title III, Part I; Section 381)

1974		1975		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
18	$1,975,000	Indefinite	18	$2,572,000

Purpose: The Lister Hill National Center for Biomedical Communications encourages the application of advanced communications and computer technology to the solution of biomedical information problems.

Explanation: The Center matches high priority needs with technological capabilities to develop experimental services and evaluate their effectiveness.

Accomplishments in 1974:

1. Satellite Communications - An experimental voice network linking over 20 native Alaskan villages with Indian Health Service hospitals continued to operate seven days a week in Alaska, utilizing a NASA Communications Satellite (ATS-1). Seven satellite telecommunications terminals were installed in the states of Washington and Alaska to support health care delivery and health education experiments using NASA's ATS-F satellite.

2. Computer-Assisted Instruction (CAI) - In FY 1974, seventy-six hospitals, medical and dental schools, and similar institutions became users of the CAI services. The national CAI network averaged over 12,000 user interactions per month.

3. Cable TV - In FY 1974 the LHC introduced the concept of "cable television for health" to the elderly population of a public housing unit in East Harlem, New York City.

Objectives in 1975:

1. Satellite Communications - In FY 1975, the ATS-1 remote medical consultation network will be expanded to support the ATS-F program. The communications link will connect native village clinics and medical centers with the Indian Health Service information service in Tucson, Arizona. The University of Washington will use the ATS-F satellite to provide education for first-year medical students at the University of Alaska, and for students taking their preceptorship under physicians in Omak, Washington.

2. Computer-Assisted Instruction (CAI) - In FY 1975 the Center will study ways to make evaluated CAI programs available for sharing by identified user populations at a most reasonable cost.

3. Cable TV - In 1975 the Center will begin an evaluation of community interaction as an effective means of health education for the geriatric population, and will begin implementing a plan to provide psychiatric services over the cable system.

NATIONAL INSTITUTES OF HEALTH

National Library of Medicine

Program Purpose and Accomplishments

Activity: National Medical Audiovisual Center (Public Health Service Act, Title III, Part I; Section 381)

1974			1975	
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
100	$2,631,000	Indefinite	100	$2,816,000

Purpose: The National Medical Audiovisual Center (NMAC) is the audiovisual arm of the National Library of Medicine. It seeks to improve basic and continuing education in the health sciences by stimulating the development and use of instructionally effective audiovisual technology. NMAC works on developmental programs in collaboration with the HRA's Office of Audiovisual Educational Development.

Explanation: The Center designs prototype audiovisual media and methods for education in conjunction with health professional school faculty and organizations; coordinates the sharing of instructional software among schools of the health professions; and disseminates information on effective instructional media through consultation and training programs.

Accomplishments in 1974: The NMAC rendered 73,000 units of educational service and assistance to institutions and individuals in the health professional community including 3,000 responses to inquiries for instructional media information. Direct services included 65,000 film loans and the sale to various institutions of 2,000 videotape duplicates of instructional programs. Technical assistance which the NMAC provided included 3,000 copies of training and technical reports, 123 site consultations and in-house working sessions, and 15 instructional media workshops.

Objectives for 1975: In FY 1975, NMAC will continue to concentrate its support in key areas of change and institutional needs such as providing direct educational services and developing new media.

Cooperation with national professional organizations and health professional school faculties will continue to provide specialized support for developing the curriculum content of audiovisual media. In addition, agreements with organizations such as the Association of American Medical Colleges and the American Association of Dental Schools will provide the NMAC with continuing feedback on the actual utility of media which have been developed.

The identification, cataloging, and indexing of instructional media will continue. Specifically, reference to available media will be enhanced through augmentation of NLM information systems. The distribution of instructional materials, whether through film loan, broadcast transmission, or videotape duplication, will be concentrated on those materials which have proven to be most valuable in furthering the health education process.

NATIONAL INSTITUTES OF HEALTH

National Library of Medicine

Program Purpose and Accomplishments

Activity: Library Operations (Public Health Service Act, Title III, Part I; Section 381)

1974			1975	
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
246	$8,859,000	Indefinite	246	$9,734,000

Purpose: Library Operations provides bibliographic, reference and loan services as the central resource for a nation-wide network of regional and local medical libraries. Library Operations compiles and publishes catalogs, indexes, and bibliographies pertinent to biomedicine.

Explanation: Library Operations selects, acquires, indexes, catalogs and preserves the world's biomedical publications. Access to the contents of these publications is provided through manual and machine-produced bibliographies, catalogs, and indexes including Index Medicus, Abridged Index Medicus, Current Catalog and 28 specialized bibliographies. Library Operations manages MEDLINE services, coordinates the Regional Medical Libraries Program, and serves as the Regional Medical Library for the Mid-Atlantic Region.

Accomplishments in 1974: FY 1974 has been characterized by continued rapid growth of MEDLINE; an expansion of the number of on-line services available; an upgrading of the equipment used; the institution of MEDLINE user charges and achievement of full operational status for the second generation MEDLARS System, MEDLARS II. During FY 1974 the number of MEDLINE users increased 50 percent to 250 and the number of searches performed increased 40 percent to 225,000. Several new data bases were added to the NLM's on-line network including: SDILINE, which is a complete file of those citations for the next month's Index Medicus; CATLINE, which contains catalog data on the monographic collection of the NLM; and SERLINE, which provides descriptive information on the 5,500 major biomedical serial titles including what libraries hold those titles. Routine library services will reach the following levels during FY 1974: indexing 225,000 articles, publishing 28 recurring bibliographies, acquiring 100,000 serial pieces and 26,000 monographs, providing 175,000 interlibrary loans and 90,000 reader services.

Objectives for 1975: During FY 1975 a major expansion of the MEDLARS data base to include author abstracts along with regular indexing will be undertaken. Inclusion of an estimated 100,000 abstracts will enable users to retrieve more specific information than is currently available. MEDLARS II with its greatly enriched vocabulary will be operational for all of FY 1975. Additional data bases will be added and the TOXLINE operation will be brought in-house. Cooperative efforts with other National and Federal libraries will be expanded in FY 1975 including a major effort with the Ohio College Library Center (OCLC) whereby the NLM will participate in an on-line cataloging system.

NATIONAL INSTITUTES OF HEALTH

National Library of Medicine

Program Purpose and Accomplishments

Activity: Toxicology Information (Public Health Service Act, Title III, Part I; Section 381)

1974			1975	
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
16	$1,563,000	Indefinite	16	$1,808,000

Purpose: The Toxicology Information Program (TIP) is responsible for developing and operating a computer-based toxicology information storage and retrieval system and issues publications and other information packages in the field of toxicology information.

Explanation: The TIP serves as a national resource for toxicological information by organizing data from diverse sources into computer-based files. It provides an on-line toxicology information service; prepares monographs, state-of-the-art reviews, and selected annotated bibliographies for publication; and performs literature search services for the scientific community.

Accomplishments in 1974: In 1974, TIP continued to develop and maintain TOXLINE (formerly called TOXICON), its on-line bibliographic information retrieval service. The system contains 300,000 records consisting of citations, index terms and abstracts from the published toxicology literature. At the end of its first year of operation, over 70 organizations were paying for the use of TOXLINE. The "Common Data Base," a computerized file containing structural and nomenclature information on biomedical compounds, has been incorporated in part into an on-line, interactive file, the TOXLINE Chemical Dictionary. This file consists of over 60,000 chemical substance records containing molecular formulas, synonyms, and other data which enable a user to search TOXLINE for information on a single chemical substance known by many names in the literature, thus greatly increasing the usefulness of all other toxicology information services. The TIP published Volume II of Drug Interactions - An Annotated Bibliography with Selected Excerpts, containing over 1,200 excerpts on drug interaction that appeared in the 1970 and 1971 literature. The program also provided input from the MEDLARS data base for the journal and companion tape service, Abstracts on Health Effects of Environmental Pollutants. The Toxicology Information Response Center at the Atomic Energy Commission's Oak Ridge National Laboratory, completed over 350 literature searches for the scientific community.

Objectives for 1975: The TIP will maintain and operate TOXLINE, performing major file updates on a monthly basis, and will maintain the TOXLINE Chemical Dictionary File, which is expected to increase in size by five to ten percent. The program will undertake the construction of a Toxicology Data Bank in TOXLINE with a goal of including biomedical and related data for 1,000 chemical substances in the file. In 1975, TIP will work to implement the directives of the DHEW Toxicology Coordinating Committee calling for TIP to manage the toxicology information activities of DHEW. Initially, TIP plans to inventory existing systems and to identify the needs of each agency for toxicology information. TIP plans to have a pilot computer system, capable of handling toxicology information and data, ready for testing during 1975.

NATIONAL INSTITUTES OF HEALTH

National Library of Medicine

Program Purpose and Accomplishments

Activity: Review and Approval (Public Health Service Act, Title III, Part I; Section 381)

1974		1975		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
27	$794,000	Indefinite	27	$824,000

Purpose: This activity provides staff to manage the six grant programs authorized by the Health Programs Extension Act of 1973, as well as international activities of the NLM funded by the Scientific Activities Overseas appropriation.

Explanation: Functions include the preparation and processing of grant applications for review committees and the Board of Regents of the National Library of Medicine. In an average year the staff handles 450 to 500 applications, one-quarter of which are non-competing renewal applications. Review and Approval also provides assistance to applicants in interpreting program policies; provides overall grants management and direction; and performs continual program planning, analysis and evaluation.

Accomplishments in 1974: In 1974 Review and Approval continued to provide grants management and program planning for the NLM's grants programs.

Objectives for 1975: The requested funding level will allow continuation of Review and Approval activities at approximately the 1974 level.

NATIONAL INSTITUTES OF HEALTH

National Library of Medicine

Program Purpose and Accomplishments

Activity: Program Direction (Public Health Service Act, Title III, Part I, Section 381)

1974		1975		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
53	$3,403,000	Indefinite	53	$3,702,000

Purpose: This activity provides the program leadership and centralized administrative support necessary for the coordinated operation of all NLM activities.

Explanation: Program Direction provides support for the immediate Office of the Director, Office of Administration, Office of Inquiries and Publications Management, and payments to the National Institutes of Health Management Fund for centrally furnished services.

Accomplishments in 1974: Program Direction gave increased emphasis to program analysis and the evaluation of NLM supported programs as was evidenced by the creation of a new Office of Program Analysis and Legislation.

Under this activity is located the overall direction and coordination of the construction of the Lister Hill National Center for Biomedical Communications. Planning funds for the architectural and engineering design of this new facility have been apportioned and a firm is engaged in this work.

Objectives for 1975: Activities in program planning and evaluation and in the coordination of Lister Hill facility construction will continue to receive major emphasis. The initial design concept drawings for the Lister Hill building have been completed and the final bid documents necessary for the actual construction will be completed by the middle of FY 1975.

TUESDAY, APRIL 2, 1974.

NATIONAL INSTITUTES OF HEALTH

BUILDINGS AND FACILITIES

WITNESSES

LEON M. SCHWARTZ, ASSOCIATE DIRECTOR FOR ADMINISTRATION, NATIONAL INSTITUTES OF HEALTH

DR. ROBERT S. STONE, DIRECTOR, NATIONAL INSTITUTES OF HEALTH

DR. DeWITT STETTEN, JR., DEPUTY DIRECTOR FOR SCIENCE, NATIONAL INSTITUTES OF HEALTH

ROSS HOLLIDAY, DIRECTOR, OFFICE OF ENGINEERING SERVICES, NATIONAL INSTITUTES OF HEALTH

LELAND B. MAY, ACTING DIRECTOR OF FINANCIAL MANAGEMENT, NATIONAL INSTITUTES OF HEALTH

CHARLES MILLER, DEPUTY ASSISTANT SECRETARY, BUDGET

Object Classification (in thousands of dollars)

Identification code 09-25-0838-0-1-651	1973 actual	1974 est.	1975 est.
NATIONAL INSTITUTES OF HEALTH			
24.0 Printing and reproduction	---------	2	1
25.0 Other services	2,916	6,474	974
32.0 Lands and structures	294	8,068	8,770
Total obligations, National Institutes of Health	3,210	14,544	9,745
ALLOCATION TO GENERAL SERVICES ADMINISTRATION			
21.0 Travel and transportation of persons	---------	1	---------
23.0 Rent, communications, and utilities	1	1	---------
24.0 Printing and reproduction	1	2	---------
25.0 Other services	151	822	46
32.0 Lands and structures	31	92	---------
Total obligations, General Services Administration	184	918	46
99.0 Total obligations	3,394	15,462	9,791

Program and Financing (in thousands of dollars)

Identification code: 09-25-0838-0-1-651	Costs to this appropriation					Analysis of 1975 financing			
	Total estimate	To June 30, 1972	1973 actual	1974 estimate	1975 estimate	Deduct selected resources and unobligated balance, start of year	Add selected resources and unobligated balance, end of year	Appropriation required, 1975	Appropriation required to complete
Program by activities:									
1. Research facilities	295,528	30,168	332	3,469	2,774	7,137	4,363	---------	254,422
2. Service and administrative facilities	60,766	21,292	805	4,131	10,708	16,320	8,612	3,000	15,218
Total program costs, funded	356,294	51,460	1,137	7,600	13,482	23,457	12,975	3,000	269,640
Change in selected resources (undelivered orders)			2,257	7,862	−3,691				
10 Total obligations			3,394	15,462	9,791				
Financing:									
21 Unobligated balance available, start of year			−12,187	−17,293	−9,831				
24 Unobligated balance available, end of year			17,293	9,831	3,040				
40 **Budget authority (appropriation)**			8,500	8,000	3,000				
Relation of obligations to outlays:									
71 Obligations incurred, net			3,394	15,462	9,791				
72 Obligated balance, start of year			4,212	6,270	13,335				
74 Obligated balance, end of year			−6,270	−13,335	−9,555				
90 Outlays			1,336	8,397	13,571				

Mr. NATCHER. The committee will come to order.

WITNESS INTRODUCTION

At this time we take up "Buildings and facilities of the National Institutes of Health. Mr. Schwartz, we will be pleased to hear from you.

We will put in your biographical sketch.

[The biographical sketch follows:]

BIOGRAPHICAL SKETCH

Name.—Leon M. Schwartz.

Position.—Associate Director for Administration, NIH.

Birthplace and date.—Baltimore, Md., April 26, 1928.

Education.—A.B., economics, Johns Hopkins University, 1950.

Experience.—Associate Director for Administration, NIH, January 1972–present; Deputy Assistant Director for Program Management, Research Applications Directorate, National Science Foundation, 1971; Assistant Commissioner for Administration, Office of Education, DHEW, 1968–71; Deputy Assistant Commissioner for Administration, Office of Education, DHEW, 1967–68; Goddard Space Flight Center, National Aeronautics and Space Administration, 1960–67; Chief of Program Review and Resources Management, 1966–67; Director of Program Support Division, 1965–66; business manager, meteorological satellite program, 1962–65; financial cost analyst, 1960–62; assistant treasurer and chief accountant, Carpel, Inc., 1954–60; part-time instructor, accounting—Pace account course, Baltimore Institute, 1958–63.

Association memberships.—Maryland Association of Certified Public Accountants.

Special awards, citations, or publications.—Certified public accountant; HEW Superior Service Award, 1970; consultant to National Science Foundation, advisory panel for the research management improvement program, 1973–74.

OPENING STATEMENT

Mr. SCHWARTZ. Mr. Chairman and members of the committee, this appropriation provides funds for design, construction, repair, and improvement of facilities for the National Institutes of Health.

In total, we are requesting $3 million in fiscal year 1975 for the following:

Repairs and improvements—plant	$1,000,000
Repairs and improvements—program	2,000,000

I will discuss each of these briefly.

REPAIRS AND IMPROVEMENTS—PLANT

These funds are needed for major repair and improvements to the physical plants at Bethesda, Md.; Poolesville, Md.; Hamilton, Mont.; Baltimore, Md., and other field stations for which NIH has the real property holding agency responsibility. The plants are quite extensive and many of the buildings and facilities have been in service over 35 years. The need is a continuing one providing for the care and upgrading of the various mechanical, electrical, and structural systems.

REPAIRS AND IMPROVEMENTS—PROGRAM

These funds are requested to establish a source of financing for miscellaneous alterations directly related to program needs which must be characterized as capital improvement. Heretofore, funding of this work has been provided from the operating appropriations of the Institutes. The work includes changes in physical facilities to accommodate revisions and new initiatives in research efforts. Examples of such needs include installation of structural members and restoration of wall and floor areas after the removal of obsolete special equipment which may have penetrated these areas; modification of animal surgery, autopsy and the like as needed to accommodate expansion of programs such as cardiovascular research; and demolition or relocation of masonry partitions to meet new laboratory layout needs.

I shall be happy to respond to any questions you may have and to supply any additional information desired for the record.

BASIS FOR ESTIMATE

Mr. NATCHER. Mr. Schwartz, is the $3 million which you are requesting for repairs and improvements based on specific projects, or is it just a ball-park estimate of how much will be needed?

Mr. SCHWARTZ. I would divide that into two areas. For the general repairs and improvements to the physical plants, the $1 million is based on our experience over a number of years which gives us a very good indication of what our needs will be.

The second category of the repairs and improvements which are program related are appearing in this appropriation for the first time. The experience here is somewhat sketchier but this is our best estimate at this time of what the potential needs will be.

We have accomplished these repairs and improvements using our Institutes' operating funds in the past and our records tend to indicate this would be sufficient for the next fiscal year.

Mr. NATCHER. Then your $3 million figure is strictly an estimate?

Mr. SCHWARTZ. That is correct, sir.

DECREASE FROM PRIOR YEARS

Mr. NATCHER. Can you tell us how much has been spent on these types of repairs and improvements in previous years, and whether or not $3 million represents an increase or a decrease?

Mr. SCHWARTZ. Perhaps the best example I can give is to go back to our history for fiscal year 1974. We had during this fiscal year a number of projects that are like the kinds of projects we would expect to fund under the repairs and improvements program. Last year we had $1 million in the physical plant account, and virtually all of these funds have been obligated. So we feel that this is about equal to our ongoing level of efforts.

Mr. NATCHER. Mr. Schwartz, go right ahead now as far as increase or decrease. Generally, is the amount that we have before the committee, $3 million, an increase or decrease over the last few years?

Mr. SCHWARTZ. This represents a decrease over the last fiscal year.

Mr. NATCHER. Fiscal year 1974?

Mr. SCHWARTZ. Yes, sir.

Mr. NATCHER. What was the figure we had for 1973? Do you have it?

Mr. SCHWARTZ. Fiscal year 1973 was $8 million.

INCINERATOR PROJECT

Mr. NATCHER. Under "Accomplishments" in 1974 you list termination of the incinerator contract. Does this mean that the incinerator was built or was this project killed?

Mr. SCHWARTZ. Mr. Natcher, this was a project that we started several years ago. After the initiation of construction you might recall there was an injunction filed because of the fact that an environmental impact statement had not been filed for the project. We stopped construction at that point.

We went through the process of filing an environmental impact statement and that statement was sent to the Council on Environmental Quality last year.

During this time, we were working very closely with the Montgomery County government concerning the details of the environmental impact statement.

They developed an idea of utilizing county funds to put together an incinerator that could be used for medical waste for all of the hospitals within the county. We feel that this could be a very satisfactory solution to our problem. So we have made no attempt to continue with the construction, but we are negotiating with the county at this time for utilization of their facilities.

Mr. NATCHER. How much has been spent on the incinerator project to date?

Mr. SCHWARTZ. We have obligated about $4.5 million. We are currently negotiating with the contractor for termination costs, and we are not quite sure what the total liability to the Government will be, but I would estimate it will be somewhere in the neighborhood of $1.5 million.

CLINICAL CENTER IMPROVEMENTS

Mr. NATCHER. For fiscal year 1974 we appropriated $3.6 million for air-conditioning and electrical improvements at the clinical center. What is the present status of this project?

Mr. SCHWARTZ. This project is being designed and we hope this year to get it under construction.

MASTER UTILITIES EXTENSION

Mr. NATCHER. What is the status of the master utilities extension project, for which we appropriated $3.4 million last year, Mr. Schwartz?

Mr. SCHWARTZ. This project is also under development. It is going well and there are some parts of it actually under construction.

UNOBLIGATED BALANCES

Mr. NATCHER. Last year you predicted an unobligated balance at the end of fiscal year 1974 of $6,385,325. This year I believe you are predicting the unobligated balance at the end of 1974 will be $9,831,642. What accounts for the difference of $3.5 million?

Mr. SCHWARTZ. This is due to the fact that several projects that we anticipated obligating funds in 1974 slipped into either fiscal year 1975 or in the case of the Tri-Service incinerator will not be obligated.

Mr. NATCHER. Give us the breakdown by project of the unobligated balance of $9,831.642 and also of the projected unobligated balance at the end of 1975 of $3,040,112.

Mr. SCHWARTZ. I can supply that for the record.

Mr. NATCHER. Yes.

[The information follows:]

The estimates of unobligated balances at the end of 1974 and 1975 were made on the basis of information available in September 1973. Since them a number of changes have occurred. Therefore, we will furnish the information as requested by project, both as it was estimated in September 1973 and as it appears at this time.

ESTIMATED UNOBLIGATED BALANCES, 1975 PRESIDENT'S BUDGET

	June 30, 1974	June 30, 1975
Air-conditioning and electrical improvements, building 10	$925, 837	
Ambulatory care facility	895, 000	$180, 000
Environmental Health Sciences Center	1, 977, 500	1, 777, 000
Improvements to blue collar work areas	271, 680	
Incinerator, Rocky Mountain Laboratory	287, 505	
Lister Hill National Center	46, 327	
Master utilities extension, phase II	4, 680, 255	680, 255
Modifications to NIH heating plant	9, 598	
NIH triservice incinerator	527, 858	52, 857
Repairs and improvements, plant	200, 000	150, 000
Repairs and improvements, program		200, 000
Reproductive and perinatal biology facility	10, 082	
Total	9, 831, 642	3, 040, 112

ESTIMATED UNOBLIGATED BALANCES

	June 30, 1974	June 30, 1975
Air-conditioning and electrical improvements, building 10	$2, 980, 000	
Ambulatory care facility	3, 580, 000	$179, 000
Environmental Health Sciences Center	677, 300	
Improvements to blue collar work areas	1, 665, 000	
Lister Hill National Center	128, 400	
Master utilities extension, phase II	3, 000, 000	600, 000
Modifications to NIH waste handling facilities	1, 450, 000	
NIH triservice incinerator	657, 000	[1] 2, 558, 000
Total	14, 137, 700	3, 337, 000

[1] Estimated recovery on termination of Triservice incinerator contracts in 1975.

PROJECTS IN PLANNING STAGE

Mr. NATCHER. There are several projects for which planning funds have been appropriated but seem to be at a standstill as far as construction is concerned. These include the ambulatory care facility, child health and human development research facility, Environmental Health Sciences Center, Fogarty International Center, Lister Hill Center for Biomedical Communications, multilevel parking facility, NIH Animal Center Phase II. Are these projects all dead, Mr. Schwartz?

Mr. SCHWARTZ. No, sir. We have completed the planning in several of the projects that you have mentioned, several others are in the process of planning or we are just initiating the planning. In no case would I consider these projects dead.

Mr. Natcher. At this point in the record if you will submit just a short statement pertaining to the status of eac one of these.

Mr. Schwartz. Yes, sir.

[The information follows:]

All design work has been completed for the following projects:

1. Child health and human development research facility.
2. John E. Fogarty International Center for Advanced Study in the Health Sciences.
3. Multilevel parking facility for the general office building.
4. NIH Animal Center, phase II facilities.

The design work for the Lister Hill National Center for Biomedical Communications has been completed through the line diagram stage and is scheduled for completion near the end of this calendar year.

The design work for the Environmental Health Sciences Center was initiated in February of this year and is scheduled for completion in December 1975.

The program of requirements and preliminary engineering studies including revisions to the NIH master plan to accommodate the ambulatory care facility have been completed. Design of the facility has not been started.

Mr. Miller. May I add this statement. This kind of question came up this morning in connection with the Lister Hill Center at the library. We are always unable in the operating budget, let's say for fiscal year 1975 or fiscal year 1976. to put in the construction funds. for all of the HEW construction projects that have been planned. The budget wouldn't tolerate that kind of money. It could easily be over $100 million. So these projects stand and wait in line. I don't know of any area where it takes longer from inception to completion than direct construction of Federal buildings and a lot of these projects are waiting in line, and I wouldn't want you to think otherwise.

Mr. Natcher. There are none in the budget at this time.

Mr. Miller. There are none in the NIH budget before you. But there are several Indian hospitals in the HEW budget before the Interior Subcommittee. We just completed a major hospital at Tuba City. We usually manage to shake loose one or two construction projects each year, but as you know every construction project costs an awful lot of money.

Mr. Natcher. Can you give me any idea what you will shake loose as far as this group I just enumerated? Mr. Patten would like to know what would be shake No. 1.

Mr. Miller. I will try to provide that for the record. I don't know in what order they are going to be ready for construction.

Mr. Schwartz. I could mention what the priorities of NIH would be. Our first priority would be the Child Health Building. We are also quite interested in the ambulatory care facility. This is at an early point in the planning and of course would not impact the construction budget for several years. Lister Hill as you heard this morning also has an extremely high priority within NIH.

Mr. Natcher. If you will, Mr. Schwartz, present for insertion in the record a current cost estimate for the completion of the projects that we have just mentioned here. Can you do that?

Mr. Schwartz. Yes: we have that information.

[The information follows:]

NIH DIRECT CONSTRUCTION PROGRAM
Estimated Project Cost and Funding
Active Projects
March 25, 1974

	Estimated Project Cost 2/14/74	Funds Appropriated Through 1974	Funds Required To Complete
Authorized Projects			
Ambulatory Care Facility	$ 66,000,000	$ 3,580,000	$ 62,420,000
Child Health and Human Development Research Facility and Multilevel Parking	25,861,500	621,500	25,240,000
Electrical and Air Conditioning Improvements, Bldg. 10	4,775,000	4,775,000	--
Environmental Health Sciences Center:			
Master Site Planning	215,000	215,000	--
Phase IA - Permanent Facilities	45,441,700	2,441,700	43,000,000
Site Development and Utilities	19,035,800	1,235,800	17,800,000
Fogarty International Center	13,100,000	500,000	12,600,000
Improvements to Blue Collar Work Areas	1,957,979	1,957,979	--
Incinerator - Rocky Mountain Laboratory	325,000	325,000	--
Lister Hill National Center	20,565,000	765,000	19,800,000
Master Utilities Extension - Phase II	14,060,000	5,870,000	8,190,000
Modifications to NIH Heating Plant	240,000	240,000	--
Modifications to NIH Waste Handling Facilities	1,450,000	1,450,000	--
Multilevel Parking - General Office Building	6,611,000	211,000	6,400,000
NIH Animal Center - Phase II	8,980,100	280,100	8,700,000
Repairs and Improvements - Plant	3,232,734	2,232,734	1,000,000[1/]
Repairs and Improvements - Program	2,000,000	--	2,000,000[1/]
Reproductive and Perinatal Biology Facility	2,405,081	2,405,081	--
Total	$236,255,894	$29,105,894	$207,150,000

[1/] 1975 Budget Request.

INCOMPLETED PROJECTS

Mr. NATCHER. Also, update the table on page 1369 of last year's hearings for us please.

[The information appears on p. 1280.]

RENTAL SPACE

Mr. NATCHER. Last year you told us that 2,381 NIH employees were housed in rental space at an annual rental cost of about $1,700,000. Is that still the case?

Mr. SCHWARTZ. It is essentially the same in terms of numbers of NIH employees in rental space. This year we have the cost of the rental facilities reflected in our Office of the Director budget. Heretofore this was an item that appeared in the GSA budget and for the first time it will be included in the NIH budget.

Mr. NATCHER. Please update the table on page 1374 of last year's hearings.

[The information appears on p. 1281.]

NIH DIRECT CONSTRUCTION PROJECTS
Uncompleted Projects
1974 and 1975

Project Title	Estimated Project Cost	Funds Provided		Obligations		
		Year	Amount	Through 1973	Estimate 1974 & 1975	Total Through 1975
Air Conditioning and Electrical Improvements, Bldg. 10	$ 4,775,000	1973, 1974	$ 4,775,000	$ 31,163	$ 4,743,837	$ 4,775,000
Ambulatory Care Facility	66,000,000	1973	3,580,000	--	3,401,000	3,401,000
Child Health and Human Development Research Facility	25,861,500	1966	621,494	602,122	19,372	621,494
Environmental Health Sciences Center	64,692,500	1961, 1965, 1970, & 1972	3,892,500	215,000	3,677,500	3,892,500
Fogarty International Center	13,100,000	1968	500,000	500,000	--	500,000
Improvements to Blue Collar Work Areas	1,957,979	1972 & 1973	1,957,979	186,299	1,771,680	1,957,979
Incinerator - Rocky Mountain Laboratory	325,000	1972	325,000	7,495	317,505	325,000
Lister Hill National Center for Biomedical Communications	20,565,000	1970	765,000	158,673	606,327	765,000
Master Utilities Extension - Phase II	14,060,000	1973, 1974	5,870,000	--	5,280,255	5,280,255
Modifications to NIH Heating Plant	240,000	1972	240,000	42,402	197,598	240,000
Modifications to NIH Waste Handling Facilities	1,450,000	1973	1,450,000	--	1,450,000	1,450,000
Multilevel Parking Facility - General Office Building	6,611,000	1966, 1967	183,568	183,568	--	183,568
NIH Animal Center - Phase II	8,980,100	1965, 1968, & 1974	280,100	265,539	14,561	280,100
NIH Tri-Service Incinerator Facility	5,131,000	1967-1973	5,131,000	4,473,145	-2,765,145[1]	1,708,000
Reproductive and Perinatal Biology Facility	2,405,081	1971, 1973	2,405,081	2,294,999	110,082	2,405,081
Total	$236,154,160		$31,976,722	$8,960,405	$18,824,572	$27,784,977

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[1] Estimated recovery of funds on termination of contracts for NIH Tri-Service Incinerator Facility.

RENTAL SPACE - WASHINGTON METROPOLITAN AREA

	OFFICE SPACE SQ. FT.	STAFFING	OTHER SPACE SQ. FT.	STAFFING	TOTALS SQ. FT.	TOTALS STAFFING	ANNUAL RENTAL FEE
Auburn Building	4,409	25	14,996	35	19,405	60	$ 103,370
Blair Building	6,835[1/]	42	--	--	6,835	42	311,987
Eye Research Foundation[2/]	309	2	1,850	8	2,159	10	17,272
Federal Building	89,718	397[3/]	15,604[4/]	1	105,322	398	Govt. Owned
Landow Building	95,183	491	4,429	--	99,612	491	470,667
Litton Bionetics[2/]	--	--	1,168	29	1,168	29	9,250
Washington Hospital Center	--	--	620	1	620	1	3,400
Westwood Building	150,833	800	16,511[5/]	24	167,344	824	747,190
Westwood Annex Building	56,055[6/]	349	--	--	56,055	349	236,121
	403,342	2,106	55,178	98	458,520	2,204	$1,899,257
Danac Warehouse	--	--	60,000	12	60,000	12	115,020
Total	403,342	2,106	115,178	110	518,520	2,216	$2,014,277

[1/] New acquisition - partial occupancy. Currently under renovation.

[2/] NIH lease figures used as opposed to other facilities which reflect GSA estimates.

[3/] Reflects current ongoing shifts of programs to and from other facilities.

[4/] Includes 15,000 square feet in parking/storage.

[5/] Increase due to adjustments in classification of space made by GSA.

[6/] Total space reduced by approximately 3,000 square feet which was credited to a valet shop and snack bar.

JUSTIFICATION OF THE BUDGET ESTIMATES

NATIONAL INSTITUTES OF HEALTH

Buildings and Facilities

Amounts Available for Obligation

	1974 Revised	1975
Appropriation	$8,000,000	$3,000,000
Unobligated balance, start of year	17,293,291	9,831,642
Unobligated balance, end of year	-9,831,642	-3,040,112
Total, obligations	15,461,649	9,791,530

Summary of Changes

1974 Budget Authority	$8,000,000
1975 Budget Authority	3,000,000
Net Change	-5,000,000

Increases:

A. Program:

1. Repairs and improvements, plant	+$1,000,000
2. Repairs and improvements, program	+2,000,000
Total, increases	+3,000,000

Decreases:

A. Program:

1. Electrical and air conditioning improvements, Building 10	-3,600,000
2. Master utilities extension - Phase II	-3,400,000
3. Repairs and improvements	-1,000,000
Total, decreases	-8,000,000
Total, net changes	-5,000,000

Explanation of Changes

Program increases: The $3,000,000 increase includes: $1,000,000 for continuation of the plant repairs and improvements program and $2,000,000 for repairs and improvements for program activities.

Program decreases: The decrease of $8,000,000 is composed of new funding provided in 1974 for: Electrical and air conditioning improvements in the Clinical Center, Building 10, $3,600,000; the Master Utilities Extension - Phase II, $3,400,000; and $1,000,000 for major repairs and improvements.

Obligations by Activity

Page Ref.		1974 Estimate	1975 Estimate	Increase or Decrease
278	Research facilities..................	$5,313,325	$ 971,909	-$4,341,416
278	Service and administrative facilities.	10,148,324	8,819,621	-1,328,703
Total obligations.........................		15,461,649	9,791,530	-5,670,119

Explanation of Changes

A) Research facilities--no new budget authority requested in 1975 and all major design contracts for this activity projected for award in 1974.

B) Service and administrative facilities - new obligational authority reduced from $8 million to $3 million in 1975. A number of construction contracts for segments of several multiphase projects scheduled for award in 1975.

Obligations by Object

	1974 Estimate	1975 Estimate	Increase or Decrease
NATIONAL INSTITUTES OF HEALTH			
Printing and reproduction	$ 2,000	$ 1,000	$ -1,000
Other services	6,473,649	974,530	-5,499,119
Lands and structures	8,068,000	8,770,000	+702,000
Total, National Institutes of Health	14,543,649	9,745,530	-4,798,119
ALLOCATION TO GENERAL SERVICES ADMINISTRATION			
Travel and transportation of persons	$ 1,000	$ ---	$ -1,000
Rent, communications, and utilities	1,000	---	-1,000
Printing and reproduction	2,000	---	-2,000
Other services	822,000	46,000	-776,000
Lands and structures	92,000	---	-92,000
Total, General Services Administration	918,000	46,000	-872,000
Total obligations by object	15,461,649	9,791,530	-5,670,119

Buildings and Facilities

Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
1965	$21,512,000	$21,512,000	$23,012,000	$22,512,000
1966	7,781,000	9,431,000	8,977,000	8,977,000
1967	18,279,000	18,279,000	18,279,000	18,279,000
1968	10,715,000	10,715,000	15,075,000	10,715,000
1969	12,495,000	---	5,310,000	---
1970[1]	1,000,000	1,000,000	1,900,000	1,900,000
1971	---	---	---	---
1972	3,565,000	3,565,000	5,065,000	3,565,000
1973	8,500,000	8,500,000	33,480,000	8,500,000[2]
1974	8,000,000	8,000,000	8,000,000	8,000,000
1975	3,000,000			

[1] Prior to 1970, funds include all DHEW health activities. Separate NIH appropriation enacted in 1970.

[2] This appropriation authority was the continuing resolution. The appropriation amount was the House Allowance, which was the lower of the House or Senate amounts in the first vetoed bill.

Buildings and Facilities, NIH

New Obligational Authority	1974 Estimate	1975 Estimate	Increase or Decrease
Research facilities	$ ---	$ ---	$ ---
Service and administrative facilities	8,000,000	3,000,000	-5,000,000
Total	$8,000,000	$3,000,000	$-5,000,000

General Statement

This appropriation includes all proposed direct construction items of the National Institutes of Health and all continuing projects including unobligated balances remaining from the Mental Health-Neurology Research Facility, which was originally appropriated under "Mental Health Activities" and "Neurology and Blindness Activities" in 1961 but excludes the John E. Fogarty International Center for Advanced Study in the Health Sciences, for which planning funds were appropriated in 1968 under "John E. Fogarty International Center for Advanced Study in the Health Sciences".

Research Facilities

Includes those facilities used directly by the research activities of the National Institutes of Health.

Service and Administrative Facilities

Those facilities which render administrative and service support to the research activities of the National Institutes of Health.

Items of Special Concern

Repairs and Improvements - Plant

1975 appropriation estimate	$1,000,000

In 1975, $1,000,000 is requested for repairs and improvements to the existing NIH plant. The NIH physical plant is quite extensive and many of the buildings and facilities have been in service over 35 years. The need for repairs and improvements is a continuing one and the funds requested in 1975 will provide for such items as the installation of animal waste handling systems, major repairs to building roofs and paved areas, and the replacement and or repair of obsolete mechanical and electrical equipment related to building utility systems.

Repairs and Improvements - Program

1975 appropriation estimate	$2,000,000

In 1975, $2,000,000 is requested to begin a new project of financing improvements related directly to program needs. This project results directly from criticism by the General Accounting Office of an earlier practice under which program-related improvements were financed from Institute operating funds. Revised procedures involving program alterations will permit compliance with all GAO recommendations.

NATIONAL INSTITUTES OF HEALTH

Buildings and Facilities

Program Purpose and Accomplishments

Activities: Research Facilities and Service and Administrative Facilities

1974 Amount	1975 Authorization	1975 Budget Estimate
$8,000,000	Indefinite	$3,000,000

Purpose: The NIH direct construction program provides for the construction, improvement and major repair of the buildings and supporting facilities essential to the conduct of the mission of the National Institutes of Health.

Explanation: Buildings and facilities funded under this appropriation include those required for both research programs and for supportive services at the main NIH reservation, Bethesda, Maryland; the NIH Animal Center, Poolesville, Maryland; the Research Triangle Park, North Carolina; and other NIH field stations.

Accomplishments in 1974:

Construction Completed
Improvements to Blue Collar Work Areas (part)

Construction Contract Terminated

NIH Tri-Service Incinerator

Construction Continued

Reproductive and Perinatal Biology Facility

Construction Contracts to be Awarded

Correction of Electrical Deficiencies, Patient Bedroom Areas, Bldg. 10
Incinerator - Rocky Mountain Laboratory, Hamilton, Montana
Master Utilities Extension (part)
Modifications to NIH Heating Plant

Design Contracts Completed

Child Health and Human Development Research Facility
Incinerator - Rocky Mountain Laboratory
Master Utilities Extension (part)
Modifications to NIH Heating Plant

Design Contracts Continued or Awarded

Lister Hill National Center for Biomedical Communications
Electrical and Air Conditioning Improvements, Bldg. 10
Environmental Health Sciences Center, Research Triangle Park, North Carolina
Master Utilities Extension (part)

Pre-Design Studies

Ambulatory Care Facility
Improvements to Blue Collar Work Areas (part)

Repairs and Improvements

Continuation of major repairs and improvements to existing plant facilities

Objectives in 1975:

Construction Completed

Incinerator - Rocky Mountain Laboratory, Hamilton, Montana
Reproductive and Perinatal Biology Facility

Construction Continued

Correction of Electrical Deficiencies, Patient Bedroom Areas, Bldg. 10
Master Utilities Extension (part)
Modifications to NIH Heating Plant

Construction Contracts Awarded

Electrical and Air Conditioning Improvements, Building 10
Master Utilities Extension (Addition to Building 34)

Design Contracts Completed

Electrical and Air Conditioning Improvements, Building 10
Lister Hill National Center for Biomedical Communications
Master Utilities Extension (Addition to Building 34)

Design Contracts Continued or Awarded

Ambulatory Care Facility
Environmental Health Sciences Center, Research Triangle Park, North Carolina
Master Utilities Extension (part)

Repairs and Improvements

Continuation of major repairs and improvements to existing plant facilities
Initiation of major repairs and improvements for program activities

Mr. NATCHER. Mr. Patten.

Mr. PATTEN. I really have no questions, Mr. Schwartz.

Mr. NATCHER. Thank you very much, Mr. Schwartz.

TUESDAY, APRIL 2, 1974.

ENERGY SHORTAGE

Mr. CONTE. Have you modified or made any construction plans because of the energy shortage?

Mr. SCHWARTZ. In-process planning related to new construction will be subject to energy conservation analysis, value analysis and life cycle costs, i.e. long-term energy utilization will be a major factor in design considerations.

Adjustments have been made to operational modes of existing buildings where major alteration to systems are not required. Other adjustments requiring major alterations are being studied.

RENTAL SPACE

Mr. CONTE. How much space does NIH rent from private owners as compared with space it occupies in federally owned buildings? Do you have cost comparisons?

Mr. SCHWARTZ. NIH occupies about 5.6 million gross square feet of space in federally owned buildings and rents about 500,000 gross square feet of space from private owners. The General Services Administration has established standard level user charges in accordance with the Public Building Amendments of 1972 (P.L. 92–313). The rates for space occupied by NIH has been calculated at $6.75 per square foot for privately owned buildings and $6.48 per square foot for federally owned buildings.

USE OF MINORITY ENTERPRISES

Mr. CONTE. How many contracts for design or construction have gone to minority enterprises?

Mr. SCHWARTZ. Minority contractors have been awarded approximately 20 contracts this year. In addition to this, several of the general contractors for NIH projects have utilized minority contractors for their subcontracts. An example is the masonry contractor who is doing the brickwork for the Reproductive and Perinatal Biology Facility.

BETTER DESIGN

Mr. CONTE. Do you have any special incentives or procedures to get better design than has been usual for Federal construction?

Mr. SCHWARTZ. Yes, we have incorporated requirements in A/E design contracts to utilize Value Analysis and Life Cycle Costing. Also in our new design contracts we are including the requirement that the A/E use a suitable computer program to analyze mechanical systems, building configurations and building materials to select systems with reasonable first cost and at the same time conserve energy.

INADEQUATE SPACE

Mr. CONTE. How does the availability of space mesh with research needs?

Mr. SCHWARTZ. The availability of Clinical Center space is far exceeded by the requirements of the Institute. No research has been turned down explicitly because of space limitations because protocols are submitted and scheduled on a space available basis The total and obvious space saturation has undoubtedly forced staff to postpone and/or modify research studies.

NIH OUTPATIENTS

Mr. CONTE. What is the number of outpatients at NIH?

Mr. SCHWARTZ. There were 66,000 outpatient visits at the Clinical Center in fiscal year 73; 70,000 outpatients visits are projected for fiscal year 74.

Mr. CONTE. What is the reason for the increased outpatient activity?

Mr. SCHWARTZ.The increase in outpatient activity is attributable primarily to the changing nature of clinical research. Biomedical research efforts have gradually been shifting towards the basic knowledge of biologic mechanisms underlying disease. The ambulatory or outpatient mode is suited to this approach because it can accommodate large clinical trial which follow patients prior to the onset of clinical complications and major illness. A recent study projected a program need for facilities to accommodate 150,000 outpatient visits per year by 1980. Recognizing this need. funds have been appropriated for design of an Ambulatory Care Research Facility and it is expected that design work will begin in fiscal year 1975. Seventy million dollars in construction funds will be required in 1976.

Mr. CONTE. What is the relative cost of inpatient versus outpatient treatment?

Mr. SCHWARTZ. The relative cost of inpatient versus outpatient treatment at the Clinical Center is approximately 9 to 1, or if the patient is lodged in a motel, approximately 4 to 1.

NATIONAL INSTITUTES OF HEALTH

OFFICE OF THE DIRECTOR

WITNESSES

LEON M. SCHWARTZ, ASSOCIATE DIRECTOR FOR ADMINISTRATION, NATIONAL INSTITUTES OF HEALTH

DR. ROBERT S. STONE, DIRECTOR, NATIONAL INSTITUTES OF HEALTH

DR. DeWITT STETTEN, JR., DEPUTY DIRECTOR FOR SCIENCE, NATIONAL INSTITUTES OF HEALTH

LELAND B. MAY, ACTING DIRECTOR OF FINANCIAL MANAGEMENT, NATIONAL INSTITUTES OF HEALTH

CHARLES MILLER, DEPUTY ASSISTANT SECRETARY, BUDGET

Object Classification (in thousands of dollars)

Identification code 09-25-0846-0-1-651		1973 actual	1974 est.	1975 est.
	Direct obligations:			
	Personnel compensation:			
11.1	Permanent positions	6,990	8,078	8,431
11.3	Positions other than permanent	455	496	504
11.5	Other personnel compensation	190	207	210
	Total personnel compensation	7,635	8,781	9,145
12.1	Personnel benefits: Civilian	673	796	838
21.0	Travel and transportation of persons	113	127	127
22.0	Transportation of things	9	6	6
23.0	Rent, communications, and utilities	289	352	4,614
24.0	Printing and reproduction	234	283	283
25.0	Other services	2,123	2,381	2,962
26.0	Supplies and materials	87	99	99
31.0	Equipment	57	57	57
	Subtotal	11,220	12,882	18,131
95.0	Quarters and subsistence charges	−7	−7	−7
	Total direct obligations	11,213	12,875	18,124
	Reimbursable obligations:			
21.0	Travel and transportation of persons	4		
25.0	Other services	4,648	9,100	9,100
	Total reimbursable obligations	4,652	9,100	9,100
99.0	Total obligations	15,865	21,975	27,224

Personnel Summary

	1973 actual	1974 est.	1975 est.
Total number of permanent positions	474	530	531
Full-time equivalent of other positions	59	60	60
Average paid employment	500	554	555
Average GS grade	8.5	8.6	8.6
Average GS salary	$14,260	$15,138	$15,473
Average salary of ungraded positions	$11,138	$12,018	$12,253

Program and Financing (in thousands of dollars)

	Identification code 09–25–0846–0–1–651	1973 actual	1974 est.	1975 est.
	Program by activities:			
	Direct program:			
	1. Research management and program services	13,971	12,875	18,124
	Total direct program	13,971	12,875	18,124
	Reimbursable program:			
	1. Research management and program services	4,652	9,100	9,100
	Total program costs funded [1]	18,623	21,975	27,224
	Changes in selected resources (undelivered orders)	−2,758	---------	---------
10	Total obligations	15,865	21,975	27,224
	Financing:			
11	Receipts and reimbursements from: Federal funds	−4,652	−9,100	−9,100
25	Unobligated balance lapsing	542	---------	---------
	Budget authority	**11,755**	**12,875**	**18,124**
	Budget authority:			
40	Appropriation	12,042	12,000	18,124
41	Transferred to other accounts	−287	−28	---------
43	**Appropriation (adjusted)**	**11,755**	**11,972**	**18,124**
46.20	**Proposed transfer for civilian pay raises**	---------	886	---------
46.30	**Proposed transfer for military pay raises**	---------	17	---------
	Relation of obligations to outlays:			
71	Obligations incurred, net	11,213	12,875	18,124
72	Obligated balance, start of year	761	1,963	728
74	Obligated balance, end of year	−1,963	−728	−815
77	Adjustments in expired accounts	59	---------	---------
90	Outlays, excluding pay raise supplemental	10,070	13,251	17,993
91.20	Outlays from civilian pay raise supplemental	---------	842	44
91.30	Outlays from military pay raise supplemental	---------	17	---------

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[1] Includes capital outlays as follows: 1973, $57 thousand; 1974, $57 thousand; 1975, $57 thousand.

NOTES

Includes $201 thousand in 1975 for activities previously financed from Departmental Management. Comparable amounts for 1973 ($201 thousand) and 1974 ($201 thousand) are excluded above.

Excludes $83 thousand in 1975 for activities transferred to Assistant Secretary for Health, 1973. Comparable amounts for 1973 ($83 thousand) and 1974 ($83 thousand) are included above.

Excludes $28 thousand in 1974 and 1975 for activities transferred to Departmental Management. Comparable amount for 1973 ($28 thousand) is included above.

Mr. Natcher. Now we take up the Office of the Director, and Mr. Schwartz, we will be pleased to hear from you at this time.

OPENING STATEMENT

Mr. Schwartz. Mr. Chairman and members of the committee, the appropriation for the Office of the Director provides for the central executive direction and management of the various programs of the National Institutes of Health. Specifically, it includes:

The Director and his immediate staff and the offices responsible for program planning and evaluation and public and scientific communications; and supporting management functions, involving budget and financial management, personnel management, contracts and grants management, and management analyses and reviews.

The functions and responsibilities of this appropriation are carried out through the offices of various associate directors and appropriate office directors with the aid of staff specialists and operating personnel.

RESEARCH MANAGEMENT AND PROGRAM SERVICES

The Director's immediate office includes his principal associates and supporting staff who assist him in directing and coordinating the extensive extramural, intramural, and collaborative programs of the Institutes and Research Divisions, and the programs of the National Library of Medicine. Staff offices responsible for program planning and evaluation and for public and scientific communications support the Director in carrying out his responsibilities for the overall direction and research management of the National Institutes of Health.

The central management and program services financed by this appropriation support not only the overall direction and management of the National Institutes of Health, but also provide a number of services to the individual Institutes and other operating components. Since most of the National Institutes of Health is located within a single geographical area, it is, therefore, expeditious and economical to provide a large number of management and program services on a consolidated central basis. These services financed through this appropriation include: budget formulation and execution, financial reporting and analysis; central accounting, voucher auditing and payment services for all of our appropriations and budget accounts; position classification and salary administration, equal employment opportunities, and a wide range of other personnel management services for over 11,000 employees; contracts and grants management services relating to more than 19,000 projects; and management studies and reviews which promote economies and efficiency of operations and insure effective application of policy and procedural controls throughout all of the operating components of the National Institutes of Health.

The increased workloads and responsibilities result from expanded research initiatives on heart and lung diseases, digestive diseases, cancer, child development, aging, et cetera, and targeted research activities to improve the Nation's health, such as cancer control, hypertension education, and sickle cell disease. These research areas are placing a heavy burden on the central management and program services and the overall program direction, planning and evaluation. It is planned to provide the necessary leadership and management services to adequately support these expanding research initiatives and targeted programs.

FACILITY RENTALS

This appropriation for the first time provides funds to reimburse GSA in accordance with Public Law 92–313. The law in effect requires each agency occupying space assigned by GSA to reimburse the GSA for the space at a rate established by the Administrator and approved by OMB. Accordingly, an increase of $4,259,000 for payment to GSA is being requested.

APPROPRIATION REQUEST

Mr. Chairman, the appropriation request for the Office of the Director is $18,124,000 for 1975, an increase of $5,131,000 over the 1974 comparable level of $12,993,000. $4,985,000 of the total increase is attributable to mandatory costs—that is, payments to GSA for facility rentals, increased payments to the NIH Management Fund, within-grade increases, annualization of the 1974 pay increases, and the like. The small program increase of $146,000 will provide increased utilization of data processing for program direction, planning and evaluation, and central management services.

Thank you. I shall be happy to respond to any questions you may have.

EMPLOYMENT CEILING

Mr. Natcher. At the beginning of the hearings, Mr. Schwartz, we had a discussion of employment ceilings, as you will recall. I understood you to say that you expected to receive an increase in your employment ceiling from the Department. Is that correct?

Mr. Schwartz. Yes, sir, that is correct.

Mr. Natcher. If you receive an increase in your ceiling, does this mean that NIH will have more positions than shown in the budget?

Mr. Schwartz. Yes, sir, that is correct. When we receive these positions, I think it would be appropriate for us to put into the record the requirement for increased budgeted positions. In a few Institutes we will exceed what currently is shown as budgeted positions.

Mr. Miller. Could I comment on that?

Mr. Natcher. Go ahead.

Mr. Miller. We will not have more positions than the Congress authorized. We will have more positions than are shown in the 1974 budget column of the budget that the President submitted last January. We will be glad to discuss with staff whether we ought to get formal approval from you for that. But we will not have more than we are authorized by the Congress.

Mr. Natcher. As far as having more positions, does this apply to both 1974 and 1975?

Mr. Schwartz. It is our understanding, Mr. Natcher, that these positions would be made available to NIH in fiscal year 1974 and therefore would become part of an increased base for fiscal year 1975.

Mr. NATCHER. Please submit a revised schedule reflecting the new employment ceiling.

Mr. SCHWARTZ. We will be glad to.

[The information follows:]

NATIONAL INSTITUTES OF HEALTH—NEW EMPLOYMENT CEILING

	1973	1974 estimated original	[1] 1974	[2] 1975
NCI	1,720	1,820	1,820	1,855
NHLI	641	656	687	656
NIDR	287	265	267	265
NIAMDD	579	551	560	551
NINDS	527	515	524	515
NIAID	604	590	599	590
NIGMS	147	153	153	153
NICHD	510	514	523	524
NEI	121	127	132	127
NIEHS	228	233	235	233
RR	75	71	71	71
FIC	53	49	49	49
Total, IRD's	5,492	5,544	5,620	5,589
NLM	456	455	465	455
OD	513	525	531	525
MF	3,326	3,265	3,373	3,284
S. & S	701	606	606	606
Total, NIH	10,488	10,395	10,595	10,459

[1] Tentative, pending review by director, NIH with each institute director.

[2] 1975 employment is currently being studied. Final decisions regarding a potential increase in employment ceiling have not yet been made.

PATIENT CHARGES AT CLINICAL CENTER

Mr. NATCHER. During the past year we have heard a good deal about a proposal to charge patients who are receiving treatment at the NIH Clinical Center. Is this proposal still under consideration?

Mr. SCHWARTZ. Mr. Natcher, the specific question of the Secretary referred to the possibility of getting third party payees to reimburse the clinical center if and when the patients received hospital services and were covered by a third party payee. We have had a number of discussions with the Secretary about this and have developed a staff paper in response to this issue. No decision has been made at this time.

CONTRACTING FOR SERVICES

Mr. NATCHER. We have also heard a good deal about proposals to contract for various services performed in the past by NIH employees. To what extent is this being done, and what are the reasons for it?

Mr. SCHWARTZ. During the development of the 1974 manpower allocations to the various Institutes, we requested and received a number of proposals that considered the possibilities of contracting services that had historically been performed by civil servants. In each case we were going to review to determine if the cost of contracting would be less than the cost of doing it inhouse. We have not progressed very far with this, Mr. Natcher, for several reasons.

One is that we have had a number of discussions with our affected employees at NIH in terms of possible impact on jobs; many of these services consist largely of low income minority population at NIH and we wanted to fully understand the impact on our employers. We feel that with the current ceiling we can conclude this fiscal year without any new service contracting.

We do intend to continue to pursue this, but I assure you we will not make any moves in this direction that would wind up with additional costs to the Federal Government.

Dr. Stone has also committed himself to the employees at NIH that part of this decisionmaking process would be to review the social implications of any action that we took.

Dr. STONE. We will, of course, find that extremely hard to measure, that is the social implications, the intangibles, but we believe extremely important.

Some employees, inadequately informed, have misinterpreted our request for proposals in looking at various areas as an intent to contract out. It was in fact an attempt on our part to understand the potential costs of contracting out, what the services would cost. So we have not made decisions.

AVERAGE GRADE RESTRICTIONS

Mr. NATCHER. From time to time we hear about restrictions on average grades and average salaries. What directives have you received from OMB and the Department with respect to average grade and average salary?

Mr. SCHWARTZ. The restrictions for fiscal year 1974 are only at the average grade level, and we have been directed by the Department to maintain an average grade for this fiscal year that would be at least equal to our average grade at the end of fiscal year 1974. So it is no longer a continual reduction. We did, however, go through a 2-year period where we had to reduce average grades. This year, it is to remain at the fiscal year 1973 level.

Mr. NATCHER. We also hear complaints from time to time that employees are not being promoted or are not being paid the salaries to which their work entitles them because of these restrictions on average salary and average grade. Do you think, Mr. Schwartz, that these complaints are justified?

Mr. SCHWARTZ. There are some cases where I think the complaints are justified. In trying to achieve this kind of stability in average grade, there are some cases where promotions are made at a slower clip than if we did not have such a restriction. We look very carefully at the classification aspects of promotions, and we feel that most of these cases are held to a minimum. But I have to admit that a program such as this could create some injustices.

RECRUITMENT DIFFICULTIES

Mr. NATCHER. For years we have heard that NIH has difficulty in recruiting and retaining topflight scientists because such people can command much higher salaries outside the Government. Do you think this problem is becoming more acute?

Dr. STONE. Yes, sir, I do. I am sure it is, particularly, as several of the Institute Directors commented, at the upper levels.

Mr. NATCHER. What suggestions, Dr. Stone, can you give the committee as to a solution of this problem?

Dr. Stone. I feel no constraint in answering that except an understanding of the Federal system. We feel we greatly need a way to keep salaries competitive at the higher levels, and I don't know how to deal with it.

Mr. Natcher. Anything else, Dr. Stone?

Dr. Stone. It is true the Uniformed Services University Medical School is going to be built across the street, and we do know that salaries there are projected to be considerably different from elsewhere in the Federal health establishment, and some precedent is already established. I think there will be invidious comparisons made, which will be bad for morale. Whether there is a way for us to go a similar route or not, I don't know.

SALARY LIMITATIONS ON GRANTEES

Mr. Natcher. Are there any limitations on the salaries which can be paid from NIH grants and contracts?

Mr. Schwartz. The policy of NIH in terms of grants and contracts is that any individual has to be paid at a rate that is consistent with the policies of that university, and we audit this very carefully to insure that staff members on Federal grants and contracts get a fairly comparable salary to tenured members under university funding.

TRAINING GRANTS AND FELLOWSHIPS

Mr. Natcher. Please update the table on page 26 of last year's hearings.

[The information follows:]

RESEARCH TRAINING GRANT AND FELLOWSHIP AWARDS, FISCAL YEARS 1973–75

[Budget authority in thousands]

	1973	1974	1975
Training grants program:[1]			
Trainee costs	[2] $53,480	[2] $71,691	[2] $31,169
Institutional costs	[2] 51,383	[2] 68,879	[2] 29,986
Total	104,863	140,570	61,155
Fellowship program:[3] Fellowship awards (predoctoral and postdoctoral level)	10,898	48,880	61,115
Grand total	115,761	189,450	122,270

[1] Funds indicated for training grants represent appropriations and awards for fiscal year shown but which were expended in next following fiscal year.

[2] Estimate.

[3] Includes Fogarty International Center fellowship programs.

Mr. Natcher. Also give us tables for 1973, 1974, and 1975 similar to the tables on page 28 and 29 of last year's hearings.

[The information follows:]

DHEW - National Institutes of Health - IRD

1975 PRESIDENT'S BUDGET (Justifications)

Fellowships and Training Grants
(Amounts in thousands)

BY PROGRAM TYPE

FELLOWSHIPS	Research Training		Predoctoral		Postdoctoral		Special		Scholars		Total	
	No.	Amount	No.	Amount	No.	Amount	No.	Amount	No.	Amount	No.	Amount
Cancer...............	926	$12,000	--	--	3	$39	1	$27	--	--	930	$12,066
Heart................	650	10,600	--	--	5	35	5	50	--	--	660	10,685
Dental...............	180	2,900	--	--	--	--	--	--	--	--	180	2,900
Arthritis............	313	4,000	--	--	--	--	2	23	--	--	315	4,023
Neurology............	229	3,432	--	--	1	9	--	--	--	--	230	3,441
Allergy..............	182	3,760	--	--	51	461	26	438	--	--	259	4,659
NIGMS................	666	10,000	6	$75	257	2,975	36	468	--	--	965	13,518
Child Health.........	282	4,000	--	--	37	306	28	375	--	--	347	4,681
NEI..................	169	2,555	--	--	4	32	3	66	--	--	176	2,653
NIEHS................	70	1,060	--	--	1	7	1	8	--	--	72	1,075
Research Resources...	18	250	--	--	1	9	--	--	--	--	19	259
Fogarty Center.......	--	--	--	--	--	--	--	--	73	$1,195	73	1,195
Total Fellowships..	3,685	54,557	6	75	360	3,873	102	1,455	73	1,195	4,226	61,155

TRAINING GRANTS	Graduate			Traineeships			Clinical Training			Scientific Evaluation		Total		
	FTE	No.	Amount	FTE	No.	Amount	FTE	No.	Amount	No.	Amount	FTE	No.	Amount
Cancer...............	347	62	$3,696	--	--	--	76	45	$2,401	--	--	423	107	$6,097
Heart................	150	40	2,000	--	--	--	--	--	--	--	--	150	40	2,000
Dental...............	169	43	3,385	--	--	--	--	--	--	--	--	169	43	3,385
Arthritis............	116	39	1,506	--	--	--	--	--	--	--	--	116	39	1,506
Neurology............	286	84	3,398	14	14	$287	--	--	--	(1)	$30	300	98	3,715
Allergy..............	336	56	4,301	--	--	--	--	--	--	--	--	336	56	4,301
NIGMS................	5,184	456	29,999	--	--	--	--	--	--	(2)	350	5,184	456	30,349
Child Health.........	630	80	6,993	--	--	--	--	--	--	--	--	630	80	6,993
NEI..................	75	30	1,959	--	--	--	--	--	--	(1)	35	75	30	1,994
NIEHS................	48	18	700	--	--	--	--	--	--	--	--	48	18	700
Research Resources...	5	4	75	--	--	--	--	--	--	--	--	5	4	75
Total Training.....	7,346	912	58,012	14	14	287	76	45	2,401	(4)	415	7,436	971	61,115*

* Excludes NLM: 41 FTE's; 4 awards; $250 thousand

DHEW - National Institutes of Health - IRD

1974 COLUMN OF 1975 PRESIDENT'S BUDGET (Includes Restoration of 1973 Funds)

Fellowships and Training Grants
(Amounts in thousands)

BY PROGRAM TYPE

FELLOWSHIPS	Research Training No.	Research Training Amount	Predoctoral No.	Predoctoral Amount	Postdoctoral No.	Postdoctoral Amount	Special No.	Special Amount	Scholars No.	Scholars Amount	Total 1/ No.	Total 1/ Amount
Cancer..............	390	$5,450	--	--	92	$736	60	$899	--	--	542	$7,085
Heart...............	380	5,500	--	--	30	310	30	400	--	--	440	6,210
Dental..............	140	2,200	--	--	15	924	7	455	--	--	162	3,579
Arthritis...........	160	2,000	--	--	137	1,074	45	548	--	--	342	3,622
Neurology...........	200	3,000	--	--	18	271	--	--	--	--	218	3,271
Allergy.............	78	1,500	--	--	109	1,580	35	572	--	--	222	3,652
NIGMS...............	335	5,000	42	$250	407	5,846	119	1,548	--	--	903	12,644
Child Health........	129	1,800	--	--	65	732	50	845	--	--	244	3,377
NEI.................	116	1,784	--	--	21	190	9	213	--	--	146	2,187
NIEHS...............	37	560	--	--	4	34	1	12	--	--	42	606
Research Resources...	11	140	--	--	12	151	--	--	--	--	23	291
Fogarty Center......	--	--	--	--	--	--	--	--	151	$2,356	151	2,356
Total Fellowships..	1,976	28,934	42	250	910	11,848	356	5,492	151	2,356	3,435	48,880

1/ Includes 680 awards and $8,807 thousand restoration of 1973 funds.

TRAINING GRANTS	Graduate FTE	Graduate No.	Graduate Amount	Traineeships FTE	Traineeships No.	Traineeships Amount	Clinical Training FTE	Clinical Training No.	Clinical Training Amount	Scientific Evaluation No.	Scientific Evaluation Amount	Total 2/ FTE	Total 2/ No.	Total 2/ Amount
Cancer..............	957	108	$9,718	--	--	--	220	75	$6,840	--	--	1,177	183	$16,558
Heart...............	700	175	12,418	--	--	--	--	--	--	--	--	700	175	12,418
Dental..............	220	43	5,626	--	--	--	--	--	--	--	--	220	43	5,626
Arthritis...........	676	221	15,018	--	--	--	--	--	--	--	--	676	221	15,018
Neurology...........	769	196	12,734	31	31	$557	--	--	--	(1)	$30	800	227	13,321
Allergy.............	790	86	7,125	--	--	--	--	--	--	--	--	790	86	7,125
NIGMS...............	6,587	456	51,446	--	--	--	--	--	--	(2)	350	6,587	456	51,796
Child Health........	995	93	11,017	--	--	--	--	--	--	--	--	995	93	11,017
NEI.................	123	49	3,822	--	--	--	--	--	--	(1)	35	123	49	3,857
NIEHS...............	346	23	3,397	--	--	--	--	--	--	--	--	346	23	3,397
Research Resources...	21	6	437	--	--	--	--	--	--	--	--	21	6	437
Total Training.....	12,184	1,456	132,758	31	31	557	220	75	6,840	(4)	415	12,435	1,562	140,570*

2/ Includes 4,690 FTE's; 152 new awards and $43,603 thousand restoration of 1973 funds.
* Excludes NLM: 78 FTE's; 9 awards; $725 thousand.

DHEW - National Institutes of Health - IRD

1973 COLUMN OF 1975 PRESIDENT'S BUDGET

BY PROGRAM TYPE

Fellowships and Training Grants
(Amounts in thousands)

FELLOWSHIPS	Research Training		Predoctoral		Postdoctoral		Special		Scholars		Total 1/	
	No.	Amount	No.	Amount	No.	Amount	No.	Amount	No.	Amount	No.	Amount
Cancer...............	--	--	--	--	61	$556	30	$432	--	--	91	$988
Heart...............	--	--	--	--	36	309	36	493	--	--	72	802
Dental...............	--	--	--	--	16	158	22	349	--	--	38	507
Arthritis............	--	--	--	--	74	593	49	585	--	--	123	1,178
Neurology............	--	--	--	--	58	509	--	--	--	--	58	509
Allergy..............	--	--	--	--	34	291	7	96	--	--	41	387
NIGMS................	--	--	152	$681	268	2,160	100	1,388	--	--	520	4,229
Child Health.........	--	--	--	--	24	202	20	268	--	--	44	470
NEI..................	--	--	--	--	30	257	27	466	--	--	57	723
NIEHS................	--	--	--	--	1	11	2	16	--	--	3	27
Research Resources...	--	--	--	--	3	27	1	5	--	--	4	32
Fogarty Center.......	--	--	--	--	--	--	--	--	100	$1,046	100	1,046
Total Fellowships..	--	--	152	681	605	5,073	294	4,098	100	1,046	1,151	10,898

1/ Research Career Awards and Research Career Development Awards transferred to Research Career Programs, Special Research Grants

TRAINING GRANTS	Graduate			Traineeships			Clinical Training			Scientific Evaluation		Total		
	FTE	No.	Amount	FTE	No.	Amount	FTE	No.	Amount	No.	Amount	FTE	No.	Amount
Cancer...............	784	97	$7,576	--	--	--	180	96	$5,324	--	--	964	193	$12,900 1/
Heart................	826	220	14,344	--	--	--	--	--	--	--	--	826	220	14,344
Dental...............	309	61	2,989	--	--	--	--	--	--	(1)	$40	309	61	3,029
Arthritis............	693	232	11,705	--	--	--	--	--	--	(1)	45	693	232	11,750
Neurology............	724	201	10,575	85	85	$1,264	--	--	--	--	--	809	286	11,839
Allergy..............	768	128	6,382	--	--	--	--	--	--	--	--	768	128	6,382
NIGMS................	3,747	446	32,650	--	--	--	--	--	--	(2)	350	3,747	446	33,000
Child Health.........	635	93	6,905	--	--	--	--	--	--	--	--	635	93	6,905
NEI..................	107	43	2,409	--	--	--	--	--	--	(1)	35	107	43	2,444
NIEHS................	228	27	1,977	--	--	--	--	--	--	(1)	18	228	27	1,995
Research Resources...	22	7	275	--	--	--	--	--	--	--	--	22	7	275
Total Training.....	8,843	1,555	97,787	85	85	1,264	180	96	5,324	(6)	488	9,108	1,736	104,863 *

1/ Pulmonary Academic Awards transferred to Research Career Programs, Special Research Grants
* Excludes NLM: 121 FTE's; 13 awards; $721 thousand.

EMPLOYEE TRAINING

Mr. NATCHER. In your budget justification, Mr. Schwartz, you state that one of your objectives for fiscal year 1975 is to improve and expand personnel services, including establishing and operating the Executive Development and Management Training Branch. Can you tell us more about this item?

Mr. SCHWARTZ. Yes, sir. This Branch consists of two programs. One is directed primarily at the executive level, the higher grades from 13 through supergrades. There has been a new initiative that originated in the Civil Service Commission, along with renewed interest at OMB, to try and provide proper development for potential executives in the Federal Government and also those who are at executive levels.

We have a number of training opportunities that are available for our executives. Some examples of this, and perhaps the most extensive training, is in Charlottesville where we have the Federal Executive Training Institute. NIH sends about eight people there every year. It is a first-rate program.

We have a number of shorter courses available for management training for our personnel, and this year we have selected within NIH eight individuals at grades 14 and 15 levels who have entered into a potential executive development program where they receive special training that fits their needs.

The other part of our training activity is directed more at the lower grades, employees at NIH, and it is here we combine our upward mobility programs with mid-level training.

We have quite an active upward mobility program that we are quite proud of. We have seen a number of successes, and we think we have improved morale as a result of that.

IMPROVED GRANT AND CONTRACT ADMINISTRATION

Mr. NATCHER. You also state as an objective for 1975 strengthening the NIH contracting and grant administration by increasing the number of appraisals conducted on institutional management of grants.

First, can you tell us more about this activity?

Mr. SCHWARTZ. Yes, sir. This is not unrelated to your previous question, Mr. Natcher. Besides depending upon the auditors to review after the fact the performance of an institution, what we are going to try to do is to go to those institutions that are relatively new in the granting and contracting business with the Government and do a thorough review of their management capability, provide them with as much technical assistance as we can as to how to manage Federal funds.

We hope by this method to prevent the kind of problems that you find only several years after the problem originally emerged. So this is an attempt before the fact and in a somewhat aggressive way to go out and try to improve the grantee management capability.

Mr. NATCHER. Submit for the record some examples of your past efforts in this area.

Mr. SCHWARTZ. We will be glad to.

[The information follows:]

STRENGTHENING NIH GRANT ADMINISTRATION THROUGH INCREASED APPRAISAL OF INSTITUTIONAL MANAGEMENT CAPABILITY

Examples of past efforts in appraisal of institutional management of grants include only reviews of institutions that have been recipients of NIH grants for several years or more. Late in fiscal year 1973 and in the first half of fiscal year 1974, reviews were made of four grantees and three third-party cooperating institutions. Three of these reviews were made prior to the award of large center grants and revealed deficiencies in implementation of NIH grants management policies and procedures as well as the need for improvement in business management practices. Technical assistance and advice was provided by the review teams to correct these problems.

Our objective in fiscal year 1975 is to perform comprehensive appraisals of the business management capability of institutions receiving NIH grants for the first time, and to do this prior to the award or very soon thereafter. These appraisals will cover every aspect of institutional management, including such intangibles as the business philosophy and standards of top level officials, the policymaking process, and overall objectives of the organization, as well as the budget planning process, financial condition, accounting and personnel procedures, etc., in order to assure the highest possible return for Government funds invested. In addition to working with the new grantees in fiscal year 1975, we plan to schedule a number of management overviews of on-going grantees—selected for various reasons—to broaden our knowledge of their management capabilities and to assist them in correcting deficiencies.

MANPOWER UTILIZATION

Mr. NATCHER. You also state the Office of the Director has continued responsibility for major management programs such as manpower utilization, Federal productivity, and management review and improvement. Can you tell us about your efforts in manpower utilization?

Mr. SCHWARTZ. Yes, sir. We have conducted a pilot program in manpower utilization. It was one of the few programs selected in HEW for dissemination as an example of what good manpower utilization studies can demonstrate. We took the extramural program of the Allergy Institute and did a fairly comprehensive review of the various functions that go into making up a typical grant program. We looked at the program structure, and the division of staff responsibilities along both the functional and program line. We were able to come up with a great deal of information about the need for manpower in implementing an extramural program. We have expanded this program this year to cover the Dental Institute in the grant program and the Cancer Institute in both the grant and contract program. We hope by this means to be able to better quantify our personnel requests to the Congress.

Mr. NATCHER. Will you submit for the record a detailed description of NIH's efforts in each of the areas I just mentioned, as well as supplying the committee with any reports you have produced for either the Department or OMB or your own internal management.

Mr. SCHWARTZ. Yes, sir.

[The information follows:]

MANPOWER UTILIZATION

The NIH manpower utilization program began in May 1972 in response to a Department initiative to improve the allocation of manpower resources. The Department goal is to review all elements of DHEW within a 4-year period through studies and reviews.

NIH already has in place a manpower resources procedure. On July 10, 1972, NIH established a top level resources management committee which conducts annual program reviews to reassess our program priorities and the manner in which we will conduct our activities in grants, contracts, intramural and collaborative research. Within the purview of this committee is the review of manpower requests and plans; grade deescalation targets; budget and long-range planning; and facilities; and space planning and utilization.

A prototype work measurement study was conducted in the grants area of the National Institute of Allergy and Infectious Diseases (NIAID) which represents the first successful attempt in the Department to measure the manpower resources needed for a grants program. NIH considers it significant that the work measurement technique used in NIAID is being expanded to the grants program in the National Institute of Dental Research and to the grants and contracts activities in the National Cancer Institute. Completion of these studies is scheduled for June, 1974.

Various bureaus, institutes, and research divisions are also conducting their own manpower surveys. We are particularly proud of the resource monitoring system in the clinical center. This system started in February 1973, to apply a manpower utilization and labor performance reporting system to each departmental entity in the 511-bed research hospital. The blood bank, nuclear medicine, diagnostic radiology, pharmacy, central sterile supply, and environmental sanitation control have been incorporated in the system. In fiscal year 1975 clinical pathology, nursing, anesthesiology and inhalation therapy will be added.

FEDERAL PRODUCTIVITY

NIH has fully participated in the Federal productivity measurement program, jointly administered by the Civil Service Commission, General Accounting Office, and Office of Management and Budget. By measurement of productivity within grants and contracts administration, printing and reproduction, library services, and computer services. NIH has been able to assist the DHEW in achieving 72.9 percent coverage of all DHEW employees. The total for all Government agencies within phase III of the study was 59.9 percent coverage.

In addition to providing the required reports, NIH has participated in several seminars conducted to discuss what actions have been taken to increase productivity within each agency.

MANAGEMENT REVIEW AND IMPROVEMENT

The management review and improvement program is based on OMB Circular A–44. The last report, covering fiscal year 1973, was prepared in accordance with draft DHEW General Administration Manual chapter 8–01, and detailed management reviews, priority improvement projects, financial accomplishments and plans, automatic data processing, management of Federal reports, productivity improvements and cost reductions. The annual management report, served to promote an annual assessment by agencies of its management review and improvement program, assisted OMB in assessing agency progress and responsiveness and consolidated interagency management review and improvement reporting requirements.

TRANSFERS TO ASSISTANT SECRETARY FOR HEALTH

Mr. NATCHER. In each of the individual Institute budgets and in your own budget request money has been transferred to the Office of the Assistant Secretary for Health to support administrative management policy developments and planning and program operation functions. This transfer of funds totals $783,000.

If the Office of Assistant Secretary for Health is performing more of the administrative and policy formulation functions once performed by NIH, why is there a need for 531 positions in your office and $18,124,000 to run your office, Mr. Schwartz?

Mr. SCHWARTZ. This consisted primarily of 39 personnel slots transfered from NIH to the Office of the Assistant Secretary. We reviewed this very carefully, and it was our judgment that the kind of services that we were going to have performed at the Assistant Secretary level would be equivalent to about 39 man-years of effort. This is a relatively small amount of the total efforts that go into the management of NIH. We feel this was consistent with the developing role of the Assistant Secretary for Health.

Mr. NATCHER. Mr. Patten.

Mr. PATTEN. I have no questions.

Mr. NATCHER. Mr. Obey.

Mr. OBEY. No questions, Mr. Chairman.

EQUAL EMPLOYMENT OPPORTUNITY EFFORT

Mr. CONTE. Will you describe NIH's present EEO effort for the record, please?

[The information follows:]

The EEO Office has been strengthened and is approaching the staffing level necessary to provide the kind of staff leadership needed to establish and maintain a viable EEO program. All the major Bureaus and Institutes have appointed full-time Equal Employment Opportunity Coordinators to assist Bureau and Institute Directors in developing plans of action to bridge the gap between EEO policy and the specificity required for implementation of a meaningful EEO program. EEO Advisory Councils or Committees have been established at NIH and Bureau/Institute levels. Much progress has been made in tying those organizations together with some commonality of purpose in order to be mutually supportive throughout the NIH. Councils and committees have served as a significant adjunct to management as an appropriate forum in which employee concerns are given priority consideration. Although not to the extent desirable, some efforts have been made on a separate Institute basis, in the appointment of an EEO Contracts Compliance Officer to monitor contracts for compliance with Executive Order 11246 and to reflect NIH's EEO posture.

In addition to upward mobility training, several Institutes have implemented or sponsored in-house training. The Clinical Center sponsors prepromotion training for nurses; the Cancer Institute developed and implemented a training course for the Research Contract Branch personnel and project officers to acquaint them with rules and regulations governing contractors' employment practices; biological laboratory technician training courses have been implemented in several Institutes which lead directly to promotions or reassignment to more rewarding and challenging positions with promotion potential; and the establishment of a skills bank from which employees have been selected for development into new career areas. Our upward mobility training program is extensive. Approximately 360 employees are currently participating in undergraduate degree programs.

Several Institutes have conducted equal opportunity seminars and conferences which included wide participation of a cross-section of employees at varying grade levels and from varying generic and ethnic backgrounds. These meetings have led to constructive recommendations, resulting in a more meaningful understanding of EEO goals and implementation thereof. Equal Employment Opportunity has been made a part of supervisory development training, with a member of the EEO staff as principal instructor. An important part of the overall training effort has been the establishment of improved response mechanisms in the Guidance and Counseling Branch. In addition to assisting employees in choosing career plans, the Branch has been helpful in developing interest in and disseminating information about the availability of training programs.

Wide publicity has been given to NIH programs in order to attract minority and women candidates. Efforts include regular and routine contact with a large number of minority and women organizations and visits to same, as well as direct participation in significant conferences across the country, where an opportunity to attract minority and women candidates is present. A more specific example of a recruitment effort is demonstrated by the Cancer Institute, where five incentive slots have been established in the Office of the Director for the selective recruitment of minorities/women in grades GS-12 and above.

A summer neural science program was initiated in 1971, at the Marine Biological Laboratory in Woods Hole, Mass., for minority and ethnic group scientists. The program was in operation for 3 years at a cost of approximately $145,000. Thirteen minority scientists, selected on a competitive basis from 13 minority colleges across the country, benefited from the program.

Efforts have been made to accommodate the unique, individualized needs of employees by adjusting working hours whenever possible. Tangential to assisting employee work schedules was the establishment of a Child Day Care Center on the campus of NIH. The center was established in June 1973, and currently operates with a staff of 10 full-time persons serving approximately 60 children. This modest beginning has done much to facilitate regular employment of several women at NIH.

The EEO Office is currently circulating a draft of the proposed NIH EEO handbook. This order will establish responsibilities, describe requirements and procedures, and establish guidance for implementation of the overall NIH Equal Employment Opportunity program. It is expected that the EEO handbook will consolidate into a single order a number of separate EEO memorandums and directives that have been issued over the intervening years. This will represent a joint endeavor between the NIH EEO Office and the Office of Personnel Management.

Based upon a reallocation of staff resources and improved reporting and compliance procedures, the NIH EEO Office has greatly improved its capabilities in the area of the timely processing of complaints of discrimination. For example, EEO counselors are now being required to report to the EEO Office on day 1 concerning each and every informal contact. Not only does this allow the EEO Office to monitor and expedite complaints from their inception, but it also increases accountability with regard to day-to-day counseling activities. Moreover, the EEO Office has greatly increased its capability to assign in-house investigation teams, as opposed to contracting for CSC investigators—which of itself added greatly to our response time. Needless to say, the status of NIH complaints in process has greatly improved over previous reporting periods.

During the period from 1971 to the present time, NIH processed 22 sex discrimination complaints, 2 filed by male individuals and 20 by females; 14 other types of discrimination complaints were filed: 1 national origin; 9 racial complaints were filed by males and 4 racial complaints were filed by females.

Of the total of 36 cases reported, 16 were submitted on the basis of promotions; 3 were based on classification and/or selection.

The number of cases reported for calendar year 1971 was 8; calendar year 1972 was 13; calendar year, 1973, 14—5 of which were transferred to ADAMHA.

NIH currently has only 4 outstanding complaints.

More recently, as a result of certain employee concerns attending the issue of contracting out services, I directed that no contracts for services be let this fiscal year that directly affect the employment status of service employees, most of whom are minority. I further insisted that all judgments on contracting out must weigh the costs in human as well as economic terms. Consequently, I am relying heavily on the EEO staff as the primary communications link to the NIH EEO Advisory Council, employee groups, and others concerned with this very vital issue.

Mr. Conte. How has the employment of minorities and women changed over the last several years in terms of total numbers in higher grades?

Dr. Stone. To answer the first part of the question, we can state that, from a minority population of 20.1 percent in 1971, we increased to a high of 24.2 percent in 1973. Suffice to say, in spite of ensuing grade restrictions and employment ceilings, we are still holding steady with a minority employment percentage this year of 23.6 percent. Female employment increased from 42.8 percent in 1971 to 43 percent in 1973, and presently stands at 44 percent of the total NIH population.

To answer the second part of the question, as of 1971, minorities represented 5.4 percent of those in GS grades 13 and above; this increased to 7.3 percent in 1973, and is presently holding steady at 7 percent. Similarly, females increased from 16 percent in 1971 to 17 percent in 1973, and it is now holding at 15 percent.

For your added information, I can supply a set of tables which address this question in a more detailed manner.

[The information follows:]

MINORITY/WOMEN EMPLOYMENT 1971–74

	Minority				Total employment				
	Male	Female	Total	Percent	Male	Percent	Female	Percent	Total
All GS (full-time permanent):									
1971	867	839	1,706	20.1	3,583	42.8	4,792	57.2	8,375
1972	1,020	1,105	2,125	22.3	3,954	41.4	5,593	58.6	9,547
1973	1,034	1,116	2,150	24.2	3,814	43.0	5,052	57.0	8,866
1974	855	910	1,765	23.6	3,277	44.0	4,211	56.0	7,488
GS–13 and above (full-time Permanent):									
1971	67	17	84	5.4	1,310	84	255	16.0	1,565
1972	84	17	101	6.1	1,388	83	275	17.0	1,663
1973	96	27	123	7.3	1,401	83	280	17.0	1,681
1974	79	19	98	7.0	1,272	85	223	15.0	1,495

MINORITIES AND WOMEN ON STUDY SECTIONS

Mr. CONTE. How has membership of minorities and women on study sections and advisory councils changed?

Dr. STONE. Minority representation in study sections increased dramatically from 3.4 percent in 1971 to 7.8 percent in 1972. It then decreased significantly to 5.2 percent during the current year. Female representation has been fairly consistent at 15 percent over the intervening years. Unfortunately, 1973 statistics were not available for this presentation. The male versus female breakdown for 1971 was likewise unavailable.

I will supply a small table which depicts the available information in some detail.

[The information follows:]

STUDY SECTIONS AND ADVISORY COUNCILS

	Minority		Total		
	Total	Percent	M, percent	F, percent	Total
1971	70	3.4			2,013
1972	157	7.8	85	15	2,015
1973	NA	NA	NA	NA	NA
1974	74	5.2	85	14	1,411

NA—Not available.

OFFICE OF INSTITUTIONAL RELATIONS

Mr. CONTE. What is the budget for the Office of Institutional Relations that handles policy on ethical issues in research?

Dr. STONE. $468,000 in fiscal year 1975.

Mr. CONTE. Has that budget had any increase over the last several years to reflect increased Congressional attention to this area?

Dr. STONE. Yes, $250,000 in fiscal year 1972; $298,000 in fiscal year 1973; and $408,000 in fiscal year 1974.

BUDGET FOR REVIEW OF RESEARCH GRANT APPLICATIONS

Mr. CONTE. What is the budget for operations connected with the review of research grant applications?

Dr. STONE. $6,395,000 directly related to the review of research grant applications.

Mr. CONTE. Do you have an estimate of how much it costs to review an application?

Dr. STONE. $550.

NIH AUDIT STAFF

Mr. CONTE. Does NIH have its own audit staff?

Dr. STONE. No.

COST OF STUDY SECTIONS

Mr. CONTE. Do you have any way of telling how much study sections would cost if you had to pay their members full salary for the time they spend?

Dr. STONE. No. There are a number of unknown variables, the principal ones being the full time salaries of the individual study section members and the amount of time each spends on application review. At the present time, study section members are paid only for the time involved in their attendance at study section meetings and/or on site visits. A conservative estimate is that the costs for study section members would at least double if they were paid on a full-time basis and for the time devoted to NIH grant activities for time in reviewing aplications and/or preparing for the detailed presentation regarding applications for which the study section member is the principal reviewer.

Mr. CONTE. How many study sections does NIH have now?

Dr. STONE. Forty-nine in the Division of Research Grants.

Mr. NATCHER. Thank you, gentlemen. The committee will adjourn until 10 in the morning.

JUSTIFICATION OF THE BUDGET ESTIMATES

NATIONAL INSTITUTES OF HEALTH

Office of the Director

Amounts Available for Obligation [1/]

	1974 Revised	1975
Appropriation	$12,000,000	$18,124,000
Proposed supplemental*	903,000	---
Subtotal, adjusted appropriation	12,903,000	18,124,000
Real transfer to:		
"Departmental Management" (For Department-wide reductions in public affairs)	-28,000	---
Comparative transfers to:		
"Office of Assistant Secretary for Health" (Transfer of administrative support activities to the Office of the Assistant Secretary for Health)	-83,000	---
"Departmental Management" (Transfer of accounting functions from the OS Working Capital Fund)	-5,000	---
Comparative transfers from:		
"Departmental Management" (Transfer of indirect cost negotiation function to the OS Working Capital Fund)	6,000	---
"Departmental Management" (Transfer to support NIH accounting operations)	45,000	---
"Departmental Management" (Transfer to support decentralization of commissioned officer corps personnel office)	155,000	---
Total obligations	12,993,000	18,124,000

[1/] Excludes the following amounts for reimbursable activities carried out by this account: 1974 - $9,100,000; 1975 - $9,100,000.

*Pay transfer

Summary of Changes

1974 Estimated obligations	$12,993,000
1975 Estimated obligations	18,124,000
Net change	+5,131,000

	Base		Change from Base	
	Pos.	Amount	Pos.	Amount
Increases:				
A. Built-in:				
1. Within-grade pay increases	---	---	---	+$140,000
2. Extra day of pay	---	---	---	+34,000
3. Bureau of Employment Compensation rate increase	---	---	---	+8,000
4. Rent, utility and service and supply rate increases	---	---	---	+6,000
5. Annualization of pay increases	---	---	---	+145,000
6. Facility rentals	---	---	---	+4,259,000
7. Payment to NIH Management Fund	---	---	---	+393,000
Subtotal	---	---	---	+4,985,000
B. Program:				
Research management and program services	531	$11,359,000	---	+146,000
Total, increases	---	---	---	+5,131,000
Total, net change	---	---	---	+5,131,000

Explanation of Changes

Increases:

Built-in -- The increase of $4,985,000 will provide $140,000 for within-grade pay increases; $34,000 for an extra day of pay; $8,000 for the Bureau of Employment Compensation rate increase; $6,000 for rent, utility and service and supply rate increases; $145,000 for annualization of the 1974 pay increases; $4,259,000 for payment to the General Services Administration for facility rentals; and $393,000 for payment to the NIH Management Fund for increased costs of centrally furnished services, such as receipt and initial review of all grant applications, computer services, maintenance of buildings and grounds, custodial services, communications, and transportation.

Research management and program services -- The increase of $146,000 will provide for increased utilization of data processing in such areas as program planning and evaluation, budget and financial management, personnel management, and research contracting.

Obligations by Activity

Page Ref.		1974 Estimate Pos.	1974 Estimate Amount	1975 Estimate Pos.	1975 Estimate Amount	Increase or Decrease Pos.	Increase or Decrease Amount
288	Research management and program services..	531	$12,993,000	531	$18,124,000	---	+$5,131,000
	Total obligations..........	531	12,993,000	531	18,124,000	---	+5,131,000

Explanation of Changes

The increase of $5,131,000 provides for $4,985,000 for built-in increases and a program increase of $146,000 for increased utilization of data processing in such areas as program planning and evaluation, budget and financial management, personnel management, and research contracting.

Obligations by Object

	1974 Estimate	1975 Estimate	Increase or Decrease
Total number of permanent positions	531	531	---
Full-time equivalent of all other positions	60	60	---
Average number of all employees	555	555	---
Personnel compensation:			
Permanent positions	$8,159,000	$8,431,000	+$272,000
Positions other than permanent	496,000	504,000	+8,000
Other personnel compensation	207,000	210,000	+3,000
Subtotal, personnel compensation	8,862,000	9,145,000	+283,000
Personnel benefits	796,000	831,000	+35,000
Travel and transportation of persons	127,000	127,000	---
Transportation of things	6,000	6,000	---
Rent, communications and utilities	352,000	4,614,000	+4,262,000
Printing and reproduction	283,000	283,000	---
Other services:			
Payment to NIH Management Fund	1,634,000	2,027,000	+393,000
Other	777,000	935,000	+158,000
Supplies and materials	99,000	99,000	---
Equipment	57,000	57,000	---
Total obligations by object	12,993,000	18,124,000	+5,131,000

Office of the Director

Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
1970	$7,930,000	$7,930,000	$7,930,000	$7,930,000
1971	10,886,000	10,886,000	10,886,000	10,886,000
1972	11,324,000	11,324,000	11,324,000	11,324,000
1973*	12,423,000	12,423,000	13,423,000	12,423,000*
1974	12,993,000	12,993,000	12,993,000	12,993,000
1975	18,124,000			

*Note: This appropriation authority was the continuing resolution. The appropriation amount was the House Allowance, which was the lower of the House or Senate amounts in the first vetoed bill.

Justification

Research management and program services

	1974 Estimate		1975		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits...........	531	$9,658,000	531	$9,976,000	---	+$318,000
Other expenses..........	---	3,335,000	---	8,148,000	---	+4,813,000
Total...............	531	12,993,000	531	18,124,000	---	+5,131,000

General Statement

The Office of the Director appropriation provides for: (1) the overall direction of the National Institutes of Health, including the immediate office of the Director and the offices responsible for program planning and evaluation, and scientific and public communications; and (2) supporting management services including financial management, personnel management, management policy and review, and grant and contract management. The 1975 budget will provide for approximately the same level of central management support and services furnished to the Bureaus, Institutes, and Research Divisions of the NIH as in 1974.

Program Plans for 1974 and 1975

Executive direction of NIH will reflect a continuing emphasis on making the NIH organization an effective instrument for furthering and coordinating programs in support of biomedical research. This involves the collection and evaluation of data, the review and analysis of program issues and proposals, the appraisal of on-going programs, the development of policy position papers and the preparation of long-range program plans, as well as the preparation of information and its dissemination to the scientific and educational communities and to the general public.

The central management services financed by this appropriation support not only the overall direction and management of NIH but also provide a number of services to the individual Institutes and the other operating components of NIH. Financial management includes budget formulation and execution, financial reporting and analysis, grant payment and settlement, and accounting and voucher auditing for over 1,000 cost centers. Personnel management provides over 11,000 employees with a wide variety of personnel services, including training and employee development, classification and salary administration, employee and labor relations, equal employment opportunities, and recruitment and placement of a great variety of professional and support jobs. Management studies and review are undertaken to promote economy and efficiency of operations and to identify possible weaknesses in policy and procedural controls. The central contracts and grants office provides policy leadership and guidance in the review and servicing of over 19,000 projects.

The requested increase of $5,131,000 consists of $4,985,000 for mandatory items and $146,000 for program. The mandatory increases are: $4,259,000 for payment to GSA for facility rentals; $140,000 for within-grade pay increases; $34,000 for an extra day of pay in 1975; $6,000 for rent, utility and service and

and supply rate increases; $145,000 for annualization of the 1974 pay increases; $8,000 for the Bureau of Employment Compensation rate increase; and $393,000 for payments to the NIH Management Fund. The program increase of $146,000 is for increased utilization of data processing for program planning and evaluation, budget and financial management, personnel management, and research contracting.

NATIONAL INSTITUTES OF HEALTH

Office of the Director

Program Purpose and Accomplishments

Activity: Research management and program services

1974		1975		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
531	$12,993,000	N/A	531	$18,124,000

Purpose: The purpose of this activity is to provide overall program direction and central management services to the Bureaus, Institutes and Divisions of the National Institutes of Health.

Explanation: The functions and responsibilities of this activity are carried out through the offices of various associate directors and appropriate office directors with the aid of staff specialists and operating personnel.

Accomplishments in 1974: The expanded research initiatives including the emphasis on targeted research activities to improve the Nation's health, such as cancer control, hypertension education, and sickle cell disease have resulted in additional responsibilities in major areas including program direction, program analysis and evaluation, research contracting and financial analysis and management. Continued efforts were made to assure that the quality and effectiveness of NIH response to the needs of the NIH mission were met. These efforts included strengthened program and policy direction and expanded program analysis and evaluation; major involvement in implementing the Department's plan for reorganizing the health agencies; expansion of the Upward Mobility Program with an associated increase in sophistication in planning and managing the Program; development of a comprehensive data book to provide the status of resources and trends of major programs and operations at NIH; increased efforts in developing and maintaining the complex programs in the financial system in order to continue to improve financial reporting; and improved quality of contract management practices to assure sound business management in administration of grant and contract programs.

Objectives for 1975: It is planned to augment the effectiveness of NIH activities and to meet the increased demands of the NIH research initiatives by continued improvement in the quality and efficiency of overall program direction and management services. Several major objectives for 1975 are: (1) Improvement in comprehensive planning, priority setting, resource allocation, and reporting and evaluation of program results; (2) Develop new channels and strengthen communication with the scientific community and improve the quality of information services provided to the public and mass media; (3) Continued refinement and improvement of financial reporting and full utilization of the Federal Assistance Financing system to pay all grants for DHEW; (4) Improve and expand personnel services including establishing and operating the Executive Development and Management Training Branch for the development of potential and current executives; (5) Strengthen the NIH contracting and grant administration by increasing the number of appraisals conducted on the institutional management of grants and by maintaining more effective relationships with the NIH contractor and grantee organizations; (6) Continued responsibility for major management programs such as Manpower Utilization, Federal Productivity, and Management Review and Improvement.

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